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Very sincerely yours,

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E-8

A TEXT-BOOK

OF

Alkaloidal Therapeutics

BEING A CONDENSED RESUMÉ OF ALL AVAILABLE LITERATURE ON THE SUBJECT OF THE ACTIVE PRINCIPLES ADDED TO THE PERSONAL EXPERIENCE OF THE AUTHORS

BY

W. F. WAUGH, M. D., AND W. C. ABBOTT, M. D.

THIRD EDITION

Revised and Enlarged

CHICAGO

THE ABBOTT PRESS

1911

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This Book

IS DEDICATED TO THOSE
WHO BELIEVE IN

"THE SMALLEST POSSIBLE
QUANTITY OF THE BEST
OBTAINABLE MEANS TO
PRODUCE A DESIRED
THERAPEUTIC RESULT."

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PREFACE

The authors of this book have long recognized the urgent necessity for a work upon Alkaloidal Therapeutics that should be as complete as the present knowledge of the subject will permit, hence this book, whose success is shown by the appearance of another edition. The physicians who practise Alkalometry, who have rejected the crudity and inexactness of the galenicals for the elegance, accuracy of dosage and activity of the active-principle remedies, are now counted by the tens of thousands, and their number is constantly increasing. And yet the "standard" textbooks generally ignore this therapeutic movement and devote no more space to this important subject than did similar books two or three decades ago—in some cases even less.

The Alkaloidal idea is "in the saddle;" its phenomenal growth, in the face of active opposition and without the "weight of authority" to give it standing, is the strongest evidence of its vitality. Its enthusiastic advocates are creating for it a rich literature, but one which is scattered through many journals and books—American and European. Works of reference must be created to collect, supplement and codify this widening stream of material, in order to make it immediately available to the Alkaloidal student and practician. This is the mission of our book: to get together from all sources all the facts obtainable concerning the alkaloids and active principles, and to present them in a ready-to-use—truly "alkaloidal" —form. That many omissions have been made we are well aware—there are limitations to the perfection of all human work—but the work may be taken as it stands as a fair digest of the topics treated.

The student or physician who becomes interested in Alkaloidal therapeutics is sure to want in his library all the available literature upon the subject. We suggest that the following books be procured: Shaller's excellent "Guide to Alkaloidal Medication;" Candler's "Every-Day Diseases of Children;" Radue's "Diseases of Children;" Redfield's "Compend of the Active Principles," and the four volumes of American Alkalometry now published.

In addition every practising physician should have the companion volume to this work, the "Text-book of Alkaloidal Practice." The practician who is provided with these books—and studies them—will gain renewed enthusiasm in his profession and more pleasure and profit in its practice.

In the preparation of this book we wish especially to acknowledge our obligations to Dr. E. M. Epstein for his painstaking research of the European literature of alkaloidal therapeutics. Nearly every page bears some impress of his able delving. We are also under a great debt to thousands of members of the *Clinical Medicine* "family," who have aided us by their rich experience and inspired us by their constant encouragement.

In the revision of the text for the present (third) edition and in the incorporation of much new material, the authors gratefully acknowledge their indebtedness to the following gentlemen: H. J. Achard, M.D., J. F. Biehn, M.D., A. S. Burdick, M. D., G. F. Butler, M. D., Professor and Head of Department of Therapeutics and Professor of Preventive Medicine, Chicago College of Medicine and Surgery (Medical Department Valparaiso University, etc.), G. H. Candler, M. D.

W. C. Abbott. M. D.
Wm. F. Waugh, M. D.

INTRODUCTION

The disdain with which drug therapeutics has been regarded of late, the neglect into which the materia medica has fallen, are easily explained: The attention of the medical profession has for the last quarter of a century been especially directed to the study of pathology. A necessary result of the advances here made has been that the point from which we look upon our patients has been transferred from the clinical to the pathologic plane. Formerly we looked upon the patient from the clinical point, considering him as a living human being whose vital functions were in a state of disorder; and we were taught by the experience of ages that certain remedies could be administered to him with a reasonable expectation of relieving the disorder and restoring him to health.

When we came, however, to see in him not so much the clinical manifestations as certain structural disorders, we asked ourselves in vain, what there was in medicine to restore the structures to a normal condition. The transfer of our previous knowledge of remedies from the old point to the new had not been made. This being the case, the profession naturally sought to employ mechanical remedies for mechanical disorders, hence the enormous development which surgery and all other forms of mechanical therapeutics have received of late.

It was, however, inevitable that this state of things would not long prove satisfactory either to the physician or to the patient. The removal of a diseased organ or apparatus does not seem desirable so long as there is any possibility of its being restored to a healthy condition. The physician does not so much have to deal with the end products of disease, the ashes of a burned-out fire, as he has with a living person whose vital functions are disordered. His failure to realize this truth has opened the way to a multitude of irregular, unprofessional, therapeutic practicians, who have in the inability of the regular medical profession to treat disease excepting by the sacrifice of the diseased organs, found means of winning the support and confidence of the public.

Objections to the non-drug methods of treatment are to be found in the fact that many of them are tedious, troublesome and

uncertain in their results, wholly empiric and experimental in their primary applications, and enormously expensive, as compared with the results of direct, or drug medication. While each of the non-drug methods has its place in therapeutics, and should be fully utilized when it offers the greatest benefit in the treatment of the patient, it is probable that in nine-tenths of the cases which resort to the physician for aid, his best resources in treatment will be found in the scientific application of drugs.

Nevertheless it is impossible to return physician or patient to the old materia medica, which has been thoroughly tried and found wanting. Had it been good enough to meet the needs it would never have been deserted by the profession and by the public. We must have something better than this, if we expect to win back the position we formerly held in the confidence of the public.

The old materia medica had manifold objectionable features, its worst fault being its uncertainty. This uncertainty was inherent in the nature of vegetable drugs, and was enhanced by the imperfections of the preparations. It seems reasonable to assert that the primary requirements of the physician in prescribing drugs are, that in the first place he should know exactly what is the disorder of function which he wishes to influence favorably by the drug; next, he should know exactly what his drug will do; third, he should know how soon the action of the drug will be manifested; fourth, he should understand what clinical phenomena shall serve to indicate that enough of the drug has been administered, and when it should be moderated or discontinued.

These simple requirements are absolutely impossible of accomplishment unless the physician is dealing with drugs which are unvarying in their action. If we employ a drug whose action may vary around the entire circle, from pure sedation on the one hand to pure stimulation on the other, each new specimen of the drug secured giving its maximum effect at some point in this circle, differing from any other preparation that may have been used, drug medication can scarcely be said to be scientific. This uncertainty has tended to render the physician pessimistic in regard to drug action, and timid in the application of his remedies. He is cautiously "trying" during the early stages of disease, experimenting to ascertain what his drug can do and how great its action will be, while in the meantime the disease becomes firmly fixed in the tissues, when it might have been dislodged by well-directed measures in the beginning.

For the active principles we claim the following advantages: First, they are uniform in strength; second, they are uniform in the quality of effects they produce; third, they are certain in the quantity of their effect; fourth, their quick solubility and absorption gives quick action; fifth, they are portable; sixth, they are easy of administration, and devoid of unpleasant and irritating effects; seventh, their exactness of dosage enables us to administer them without weights, scales or other measures; eighth, the perfection with which their action has been worked out experimentally, allows their strictly scientific application; ninth, they do not deteriorate with age in any climate, active principles combined with pure sugar of milk retaining their strength unimpaired after twenty years; tenth, from the active principles we obtain effects which are impossible from the older preparations; eleventh, since the active principles exert their effects uniformly, and these are known to the physician, it is an easy matter to instruct a patient or an attendant of ordinary intelligence to administer them properly.

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PART I

CHAPTER I

Is There A Rational Basis For A Scientific Therapy?

That galenical therapeutics is satisfactory no one would for a moment contend. The practice is unsettled, the theory nebulous. The most emphatic condemnation of the one, and the most caustic criticism of the other, pass unanswered—because unanswerable—and the higher the attainments, the more illustrious the character of the critic, the more pronounced is his disparagement of the drug therapy of the present day. It is unnecessary to adduce examples of these statements; they will recur to the recollection of every physician versed in the literature of his profession.

Every work on therapeutics bewails the lamentable fact that the basis of the art is almost exclusively empiric. What does the word mean, exactly? The Standard Dictionary tells us that empiric "is relating to or based on experience or observation;" and secondly, "relying on or guided by experience or observation rather than scientific knowledge; generalizing from limited facts; hence, charlatanic." The prevalent opinion as to the readers of certain quasi-medical journals is contemptuously expressed by saying that they are men who ask solely for "something good for mumps!"

Evidently, in view of the acknowledged unreliability of strictly personal observations in the sick-room, when there is no foundation of pathological knowledge on the part of the observer, no perception of the influence of suggestion or appreciation of the natural course of disease and its tendencies, there must be a better basis for our practice, if it is ever to rank as a science.

Hitherto the criticism has been almost entirely destructive. Headland, in his "Action of Medicines," showed the fallacies of the commonly admitted theories, but his attempts at reconstruction were unsatisfactory, and in fact difficult of comprehension, because his ideas were not clearly developed in his own mind. Anstie, in his fine work on "Stimulants and Narcotics," showed that he clearly apprehended the crudeness of the old system. He stripped off the verbiage and showed that there had been simply

a change in the words designating the ideas, but that each generation had clung to the thought expressed by the phrase—"bleed down to the brandy point and brandy up to the bleeding point." Stimulation and sedation—the profession stopped with the comprehension of this elementary principle—and each new generation renamed it but clung to the idea.

Nevertheless, Anstie also failed to mend matters materially. Both the authors quoted were hampered by the imperfections of their physiologic and pathologic knowledge, and by the absence of a line of definite, uniformly-acting remedial agents. No certainties can possibly be founded upon uncertainties. Anstie studied neuralgias all his life, and enlarged our knowledge by his observations and acute reasoning, but he never appreciated the existence of that master key—autotoxemia.

Since his time an enormous quantity of work has been done in the line of experimental therapeutics. Driven of necessity to the alkaloids and other active principles to find uniformly acting agents from which to obtain uniform results, the workers in this department have supplied us with a wealth of data concerning these remedies, which for scientific precision can not be equaled by anything published upon the galenics. We *know* what atropine can do; we guess what belladonna will probably, hyoscyamus may possibly, accomplish. But as yet these researches have not been utilized; they have made but little impression upon the practice of the masses of the profession. Why is this?

We are met by the difficulty that these researches and the ordinary practice of the profession do not meet. Like two tunnels run under a mountain from opposite sides, badly designed, they fail to meet at the appointed place for junction. It is a case of bad surveying—and the fault lies with the clinical end of the line.

We have been taught to attack a disease through its name. Certain groups of phenomena have been associated under certain designations, and are known to us as cancer, pleurisy, Bright's disease, phthisis, etc. Few of the affections thus named are true pathologic entities, and their titles are only employed by the more learned as conveniences. But they are distinct species to the rank and file, and most efforts at treatment are mainly directed toward finding "specifics" which may be applied to each of these various named diseases. And yet, nothing is more certain than that comparatively few such maladies admit of any "specific" treatment, for many of them may require remedies whose action is exactly the opposite of that of drugs exhibited at other times—

such change of medication often being called for in the same case. Despite this universally admitted fact, the books of prescriptions contain hundreds of formulæ directed against diseases by their names. This lamentable mistake has sidetracked therapeutics and prevented the utilization of the priceless researches of the experimenters.

The remedial agents that have been scientifically studied and whose powers have been most strictly defined are not specific remedies for diseases but for conditions. We have agents that exalt and others that depress certain functions—it is up to the physician to ascertain in each case what functions of his patient's body need stimulation or depression, and to apply the proper remedies. The more complete his knowledge of the physiologic workings of the human body, of the alterations caused by disease, and the more precise his adaptation of therapeutic measures to the desired ends, the more nearly he approximates the ideal of scientific medicine. These propositions are axiomatic—there can be no discussion of them. The main point lies in this query: Have we such a wealth of remedial agents that can be applied with scientific precision, as will enable us to base upon it a system of practice that embraces the whole wide field with all its multifarious conditions and needs? To this we answer, no—not at present. This work is far from being completed; but it has progressed sufficiently to give us a firm foundation on which to build.

The writers of this book have spent years in collecting from all sources, books, monographs, pamphlets, journals, etc., in all the languages of the civilized world, the data available for this work. One hundred and fifty-five remedies are considered, alkaloids, glucosides and chemical substances, these being all on which sufficient information could be gathered to entitle them to consideration. Of some of these a measurably complete account is given, from which the reader can obtain copious information as to the effects of the remedy in health and in disease; while in the case of others the material is scanty and obscure, and these are included because, what little is known seems to indicate the probable value of the drug and the wisdom of giving it further attention.

Add to these the sera and the really valuable synthetics that have received corresponding study, and we have a number of remedies whose powers are known to us as far as the knowledge of human physiology permits. To this extent, there is, therefore, at last a scientific basis for therapeutics, in that we may reason from

a tolerably exact knowledge of what powers our remedies possess, and apply them to the pathologic conditions in which such powers are curative. We can affirm positively that the wealth of this material is sufficient to warrant the physician in shifting his ground from the old empiric list to these, and employing them as the rule, simply using the older remedies and methods in the exceptional instances where the applications of the exact agents have not been ascertained. The more generally this change shall be made, the more rapidly will these gaps be filled in.

To those who have given little attention to this matter the change may seem a small one—simply the substitution of a somewhat better line of preparations for those hitherto in vogue. Make no mistake—it is a revolution, a renaissance in therapeutics. The use of therapeutic certainties, accurately adapted to accurately appreciated needs, marks the appearance of a new era, the development of a new species of physicians.

The man who uses such highly specialized remedies must needs equally specialize his appreciation of the pathologic conditions presenting in each case; and that means a more careful investigation and closer watchfulness of his patient. Certainly this is not a matter for regret! Moreover, the physician will surely form the habit of early and vigorous intervention in acute maladies, since he will recognize the circulatory disturbance ushering in these attacks, and he knows the remedies that will restore normal circulatory equilibrium—and he will become an advocate of such early and decisive intervention. There will be acquired with the habit of accurate and decisive medication, that of accurate and decisive thinking—and again we say this is not a matter to be regretted!

There is already manifest a vitality and vigor in that section of the profession who have adopted this scientific therapy, that may convey a lesson. Therapeutic nihilism is unknown here; expectancy and pessimism have been ejected, and a vigorous, active optimism replaces them. There is a certain consciousness of power under that alert face, which inspires confidence in the doctor himself. It's a renaissance—a re-birth—sure enough.

CHAPTER II

Alkalometry: Active-Principle Therapeutics

WHAT IT IS

1. The administration of small doses of the most active and potent known remedies (chiefly alkaloids and other active principles representing the majority of all the accepted vegetable remedies) at short intervals until either as *remedial effect* or as signs of *drug sufficiency*, the full physiologic effects of the drug are apparent.

2. The exhibition of such doses in the form of tiny soluble granules or tablets—each containing a definite amount, usually gr. 1-134, 1-67, 1-6 or 1-3 of the drug; Gram 0.0005, 0.001, 0.01, 0.02.

3. The additional use of such solvents, eliminants, vital incitants and local and systemic antiseptics as have proved by laboratory research and extensive clinical test to be of considerable remedial value.

4. The freedom to use any and all remedial agents—always in the purest and most concentrated form available—that will produce definite results in a recognized condition.

5. The absolute avoidance of promiscuous formulas, problematic remedies, crude (vegetable) drugs and nauseous, changeable, alcoholic tinctures and fluid extracts, when the active remedial principle of the drug can be given in its purity in effective well-established dose.

WHAT IT DOES

1. It cures, where it is possible to cure, ***cito, tuto et jucunde.*** Its chemistry is done outside the sick body.

2. It gives the maximum obtainable results in the shortest possible time, with absolute safety and with no possibility of underdose, overdose or cumulative effect.

3. It enables the practician to give the most potent medicines to the youngest infant or the most squeamish invalid without the aid of scales, measures or menstrua.

4. It enables the doctor to push a remedy *to effect* without wondering whether he has poisoned that particular patient in his effort to give enough.

5. It makes it possible for the practician to have always with him an emergency case filled with standard medicaments of unchangeable strength and consistency for acute cases and urgencies,

thus enabling him to treat conditions when they most need treatment and when he can do the most good.

6. It enables the doctor to practise the most certain, safe and efficient method at a nominal cost.

7. It eliminates "chance" and, with perfectness of diagnosis and application, makes medicine "An Exact Science"—or as near that as it is possible to attain.

CHAPTER III

What We Replace

If the Galenic therapeutics were satisfactory there would be no reason for advocating a change. Its use has not been satisfactory, in any particular, and the retention of these ancient medicaments, crude, uncertain, unpleasant, has effectually nullified every effort to reduce the art to a science, and given rise to the therapeutic nihilism that has paralyzed the medical profession for the past era. It has seemed that the higher the standing of the physician, the greater has been his contempt of drugs. To illustrate this I shall quote a few expressions of prominent members of the medical guild, all which refer exclusively to the antique medicaments we seek to replace by weapons more in accord with modern needs.

John Mason Good: The science of medicine is a barbarous jargon. My experience with materia medica has proved it the baseless fabric of a dream, its theory pernicious, and the way out of it the only interesting passage it contains. The effects of medicine on the human system are, in the highest degree, uncertain, except, indeed, that they have destroyed more lives than war, pestilence and famine combined.

Dr. Evans, F. R. C. P., London: The popular medical system is a most uncertain and unsatisfactory system. It has neither philosophy nor common sense to commend it to confidence.

Marshall Hall: Let us no longer wonder at the lamentable want of success which marks our practice, when there is scarcely a sound physiological principle among us.

Prof. Gregory: Gentlemen, ninety-nine out of every hundred medical facts are medical lies, and medical doctrines are, for the most part, stark, staring nonsense.

Dr. Eliphalet Kimball: There is a doctorcraft as well as priestcraft. Physicians have slain more than war. The public would be better off without professed physicians.

Valentine Mott: Of all sciences, medicine is the most uncertain.

Marshall Hall: Thousands are annually slaughtered in the quiet sick-room.

Sir Astley Cooper: The science of medicine is founded on conjecture and improved by murder.

H. C. Wood: What has clinical therapeutics established permanently? Scarcely anything.

Dr. Ramadge, F. R. C. S., London: It cannot be denied that the present system of medicine is a burning shame to its professors —if indeed a series of vague and uncertain incongruities deserves to be called by that name. How rarely do our medicines do good! How often do they make our patients really worse! I fearlessly assert that in most cases the sufferer would be safer without a physician than with one. I have seen enough of the malpractice of my professional brethren to warrant the strong language I employ.

Prof. A. H. Stevens: The older physicians grow, the more skeptical they become of the virtues of medicine, and the more they are disposed to trust to the powers of nature.

Dr. Talmage, F. R. C. S.: I fearlessly assert that in most cases our patients would be safer without a physician than with one.

Alonzo Clark: Every dose of medicine diminishes the patient's vitality. In their zeal to do good, physicians have done much harm. They have hurried thousands to the grave who would have recovered if left to nature.

Wakley (*Lancet*): A system of routine or empirical practice has grown up, vacillating, uncertain, and often pilotless, in the treatment of disease.

Horace Green: The confidence you have in medicine will be dissipated by experience in treating disease.

Dr. Coggswell (Boston): It is my firm belief that the prevailing mode of practice is productive of vastly more evil than good, and were it absolutely abolished, mankind would be infinitely the gainer.

Prof. B. F. Parker: Instead of investigating for themselves, medical men copy the errors of their predecessors, and have thus retarded the progress of medical science and perpetuated error.

Prof. Jamison (Edinburgh): Nine times out of ten our miscalled remedies are absolutely injurious to our patients suffering from diseases of whose real character and real cause we are most culpably ignorant.

Sir John Forbes, F. R. C. P., London, Physician to the Queen: No systematic or theoretic classification of diseases or therapeutic agents ever yet promulgated is true, or anything like truth, and none can be adopted as a safe guidance in practice.

Oliver Wendell Holmes: Mankind has been drugged to death, and the world would be better off if the contents of every apothecary shop were emptied into the sea, though the consequences to the fishes would be lamentable.

James Johnson, F. R. S.: I declare as my conscientious conviction, founded on long experience and reflection, that if there was not a single physician, surgeon, man-midwife, chemist, apothecary, druggist nor drug on the face of the earth, there would be less sickness and less mortality than now prevails.

Dr. Abercrombie, F. R. C. P., Edinburgh: Medicine has been called by philosophers the art of conjecturing, the science of guessing.

Benj. Rush: The art of healing is like an unroofed temple—uncovered at the top and cracked at the foundation. I am incessantly led to make apology for the instability of the theories and practice of physic. Dissections daily convince us of our ignorance of disease, and cause us to blush at our prescriptions. What mischief have we not done under the belief of false facts and false theories? We have assisted in multiplying diseases; we have done more, we have increased their fatality.

Henle: Medical science at all times has been a medley of empirically-acquired facts and theoretical observations, and so it is likely to remain.

Magendie: Medicine is a great humbug. I know it is called a science—science, indeed! It is nothing like science. Doctors are mere empirics when they are not charlatans. We are as ignorant as man can be. Who knows anything in the world about medicine? I know nothing in the world about medicine, and I don't know anybody that does know anything about it. I do not hesitate to declare, that so gross is our ignorance of the real nature of the physiologic disorders called disease, that it would perhaps be better to do nothing and resign the complaint we are called upon to treat to the resources of nature, than to act, as we are frequently called upon to do, without knowing the why and the wherefore of our conduct and its obvious risk of hastening the end of the patient.

A. C. Bernays: Ninety-five out of every hundred patients who apply at a doctor's office to be treated would get well anyway, if left to nature.

These expressions could be extended indefinitely. Granting that some of them are the words of surgeons who knew little or nothing of therapeutics, and had a financial interest as competitors in detracting the physician, there remains a large substratum of truth in these views of the therapeutics of the day. And it is this mass of uncertain, inefficient and perilous practice that we are so earnestly combating, and seeking to replace with a materia medica founded on certain and uniform agents, whose uses have been determined by scientific experiment and confirmed by clinical trials. Two obstacles confront us—the blind faith of those who believe in the older drugs and the skepticism of those who have discovered their worthlessness and refuse to believe there are better ones. The lowest and the highest layers of the profession are out of sympathy with us; the great middle 80 percent who have detected the untrustworthy nature of the old and yet retain faith in the possibility of a better, are with us.

The others are fully aware of the fatal defects in the usual practice, but refuse to believe it can be bettered. So many "new remedies" have been urged on them that have not justified the claims made for them, that pessimism has become confirmed—and as physicians these men are worthless. In the laboratories they have their uses, but unfortunately their lack of interest in practice —and of patients—leaves them too much surplus time and they enter the teaching corps. Here they inoculate their pupils with the virus of unbelief and do-nothingism, and strengthen the ramparts of wrong. Had we the billions of Standard Oil we would place each of these men—and that means nine-tenths of the college professors—in nice sinecures or really useful places where they would be so well paid that they would desert the ranks of medicine altogether. This would clear the field for those who still have a glowing faith in their art, who love it and would not surrender the privilege of lessening the huge burden of human woe to occupy the throne of a Rockefeller. For there is no place in medicine for the pessimist. In the sick-room he is a disaster; his visit is a burden, his departure a relief. That one must die some time is known and felt by every human being; but it is an unspeakable comfort to know that a competent physician is fighting to keep you alive to the last possible moment; that you are not defrauded of a day by the ignorance or the indifference of the man you are paying to aid you. Give us the doctor who takes every chance even if he is not sure and it is only a chance. We have no use for the unbeliever, who does not know anything and does not trouble to find out.

CHAPTER IV

Sources of Information

Some explanation may be necessary as to the basis on which eclectic, homeopathic and other non-regular therapeutic suggestions are admitted to this work. The authors beg to disclaim emphatically any suggestion or thought that they are teaching "regular," eclectic, homeopathic, or any other form of medication, except just simply therapeutics. These two sectarian schools have devoted themselves specifically to the study and treatment of disease as seen under its clinical aspects. They have largely left the study of pathology to the regular school, confining themselves to that aspect of the work which is represented by the physician at the patient's bedside, studying the conditions presenting themselves, and endeavoring to apply such remedies as would obviate the disease conditions. As with all other specialists, they have made certain advances in this particular line; and we believe it is of the utmost importance to the general practicians of medicine that they should avail themselves of the results of these studies. It may be said, since the conclusions there reached are not based on pathologic certainties, but on the less reliable clinical manifestations, that such suggestions are not as reliable as those which are based on the ordinary careful pathologic laboratory investigations. We will not stop to discuss the question as to whether living physiology or dead anatomy offers the best indications for the successful application of remedies in the treatment of disease. We will simply say that our own standpoint is that of the doctor, who is seeking in every possible way to benefit his patient. It makes no difference whence the suggestion comes, if it proves beneficial. All that he cares for is that it *shall* be beneficial.

In studying the work of these schools we find an enormous mass of therapeutic suggestions drawn from clinical experience. We present these to our readers exactly as we get them. We present them for what they are worth. We do not present them as the deductions of our own experience or reasoning; but whatever good there may be in them, we need it. We would be failing in our duties to our patients, if we did not avail ourselves of everything coming from these sources, as well as from all others, that will aid us in giving them relief.

Fifty years ago such a declaration would have been sufficient to place the writer outside the pale of regular medicine. Twenty-five years ago, when Bartholow's book appeared, physicians were

amazed at the wealth of therapeutic suggestions therein contained. This great therapeutic teacher had not the courage to tell the profession how large a proportion of these suggestions was taken from eclectic works. At that time it would probably have killed his book and ruined his own prospects. The world has progressed since then, and we do not feel that it requires any special courage on our part to quote Lloyd, King, Webster, Ellingwood, and others who have done good work in this school, and given it a respectable standing in the eyes of all those who are familiar with their work.

Most of this material is practically unknown to authors of textbooks on therapeutics in the regular school. No investigation worthy of the name has been given to the great majority of the plant-remedies of America. Most investigators have contented themselves by attributing to "tannic acid" the effect of the plant, when they discovered that this agent was present in it. No proof was proffered as to the correctness of this assertion; in fact no pains were taken to ascertain whether it was true or not. The easy explanation relieved these gentlemen from the irksome task of making a genuine investigation, and of deciding the somewhat debatable question as to whether it was judicious to give credit to an eclectic writer.

We believe that the sentiment of the medical profession today is in the vast majority of instances similar to our own, that is, we can not afford to lose the benefit of anything which will help us in our work; and if these gentlemen have developed agents which are of value in the treatment of the sick, there is no reason why they should not have credit for the good work they have done. At any rate such a position is *honest;* honest to ourselves, honest to our patients, and honest to the eclectic; and that being the case, we really need not worry ourselves with the question whether a few of our brethren, in whom the memory of the old school conflicts still remains, may disapprove.

CHAPTER V

Comparative Dosage of the Active-principles and the Galenics

We have been urged many times to prepare a statement showing the relative activity of the active principles and of the galenics so that those who might desire to substitute the active principles for the older preparations could form an idea of the proper dosage,

in making the substitution. We have always refused to do this for several reasons.

The use of these remedies renders it possible for us to absolutely regulate the dosage in each instance, by the reaction of the patient to the medicine, and this is so earnestly to be desired that it would be wise if the old dosage were forgotten, and the physician could take up the active principles as absolutely new remedies, to be used in the strictly scientific manner which they now for the first time render possible. Besides, it is not easy to compare an absolute, uniform, unchanging remedy with one which is neither absolute, uniform nor unchangeable.

All fluid preparations like tinctures and fluid extracts are surely liable to two continuous processes, a degeneration by which the active principles are gradually converted into inert coloring matter and other decomposition products, by which the strength of the preparation is progressively impaired; besides, the evaporation of the alcohol and water either concentrates the remedy rendering it stronger, or induces precipitation of the active principles. So that in any special instance the strength of the preparation depends upon a balancing of these alterations, and the fact is that the only way to ascertain the exact dose of the preparation is by trying it on the patient.

If one has time to do this, all well and good, but in emergencies the result is so unsatisfactory that the users of the galenics do not put much dependence in drug medication. It is not without reason that those who use active principles believe in their power to jugulate acute maladies in their incipiency, and that those who do not use the active principles are skeptical of the possibility of such action.

However, the demand for some indication of the sort is so general that I have prepared the following data. In this the active principles of standard quality are compared with fluid extracts and tinctures of full U. S. P. strength, standardized at the time they leave the factory. This applies only to such preparations as come from the very best manufacturers. Even so, the comparison is only relative and we frankly believe is more likely to lead to perplexity than otherwise.

Take for instance juglandin: According to the best authorities the standard granule of juglandin, containing 1-6 of a grain, corresponds to two minims of the fluid extract of juglans. But the best fluid extract of juglans we have tested is recommended by its manufacturers in doses of 30 to 60 minims as a mild laxative, while

we have frequently procured a satisfactory laxative effect from 2-3 of a grain of juglandin. This would indicate that the latter is in power very much superior to the corresponding dose of the fluid extract, even accepting the latter at its manufacturer's valuation.

Possibly the fluid extract contains another active principle whose astringency antagonizes the laxation induced by juglandin. But why should we swallow 29 1-3 grains of unnecessary dirt for the sake of the 2-3 grains of desirable medicine?

With these explanations we present the list. After all it is only tentative, and we are ready to receive suggestions for its correction from those who have made any observations along this line.

Aconitine (Abbott)	gr. 1-134	equals	tincture aconite	m.	2.8
Aletrin	" 1-6	"	fl. ext. aletris	m.	5
Alnuin	" 1-12	"	" alnus	m.	1 1-4
Aloin	" 1-12	"	aloes socotrine	gr.	1
Anemonin	" 1-134	"	fl. ext. pulsatilla	m.	1
Apocynin	" 1-12	"	fl. ext. apocynum	m.	5
Arbutin	" 1-6	"	fl. ext. uva ursi	m.	2 1-2

Arsenate strychnine contains 15.4 percent of arsenic, 29 percent of arsenic acid
" iron " 27.4 " " 50 " " "
" quinine " 8. " " 15 " " "
Arsenite copper " 34. " " 56 " arsenous "
Arsenic bromide " 24.5 "
" iodide " 16.4 "
" sulphide " 69.4 "
Arsenate sodium " 24. " " 44.8 " arsenic acid
" potassium " 34.4 " " 69 " " "
" antimony " 11. " " 20 " " "
" strychnine " 64.7 " strychnine.

Asclepidin	gr. 1-12	equals	fl. ext. asclepias	m.	2
Asparagin	" 1-67	"	" asparagus	m.	1-2
Aspidospermine	" 1-67	"	" quebracho	m.	1-2
Atropine sulph.	" 1-250	"	tinct. belladonna	m.	2 1-2
Avenine	" 1-67	"	tinct. avena	m.	10
Baptisin	" 1-12	"	fl. ext. baptisia	m.	2
Barosmin	" 1-6	"	" buchu	m.	2 1-2
Berberine	" 1-6	"	" berberis	m.	10
Boldine	" 1-67	"	" peumus	m.	2
Brucine	" 1-134	"	tinct. nux vomica	m.	1-2
Bryonin	" 1-67	"	fl. ext. bryonia	m.	1
Cactin	" 1-67	"	tinct. cactus	m.	1-2
Camphor monobrom.	" 1	"	potass. bromide	gr.	10
Cantharidin	" 1-5000	"	" cantharides	m.	1
Capsicin	" 1-134	"	" capsicum	m.	1 1-4
Caulophyllin	" 1-6	"	fl. ext. caulophyllum	m.	7
Chimaphilin	" 1-6	"	" chimaphila	m.	2 1-2
Chionanthin	" 1-67	"	" chionanthus	m.	1-2
Cicutine hydrobromide	" 1-67	"	" cicuta	m.	1-2
Cocaine	" 1-134	"	" coca	m.	1-3
Codeine	" 1-6	"	opium	grs.	2
Colchicine	" 1-134	"	fl. ext. colchicum root	m.	3
Collinsonin	" 1-6	"	fl. ext. collinsonia	m.	2
Colocynthin	" 1-134	"	comp. ext. colocynth	gr.	1-6
Condurangin	" 1-67	"	fl. ext. condurango	m.	2 1-2
Convallamarin	" 1-12	"	" convallaria	m.	2
Cornin	" 1-6	"	" cornus florida	m.	2 1-2
Corydalin	" 1-6	"	" corydalis	m.	2 1-2

Cotoin	gr.	1-67	equals fl. ext. coto	m.	1·5
Cubebin	"	1-67	" " cubeb	m.	1
Cypripedin	"	1-12	" " cypripedium	m.	2 1-2
Digitalin	"	1-67	" tinct. digitalis	m.	2 1-2
Dioscorein	"	1-6	" fl. ext. dioscorea	m.	2 1-2
Delphinine	"	1-67	" " delphinium	m.	1
Duboisine	"	1-500	" " duboisia	m.	1
Echinacea conc.	"	1-2	" tinct. echinacea	m.	10
Elaterin	"	1-67	" elaterium	gr.	1-25
Emetin	"	1-67	" fl. ext. ipecacuanha	m.	2
Emetine	"	1-67	" " ipecacuanha	m.	22
Ergotin	"	1-6	" " ergot	m.	2
Euonymin	"	1-6	" " euonymus	m.	5
Eupurpurin	"	1-6	" " eupatorium purpur	m.	2 1-2
Gelseminine	"	1-250	" " gelsemium	m.	1
Gelsemin	"	1-134	" " gelsemium	m.	1-16
Geranin	"	1-6	" " geranium	m.	1
Gossypin	"	1-6	" " gossypium	m.	2
Hamamelin	"	1-6	" " hamamelis	m.	1
Helenin	"	1-6	" " elecampane	m.	30
Helonin	"	1-6	" " helonias	m.	5
Hydrastin	"	1-6	" " hydrastis	m.	1-3
Hydrastine	"	1-67	" " hydrastis	m.	2-3
Hyoscyamine	"	1-250	" " hyoscyamus	m.	2
Iridin	"	1-12	" " iris versicolor	m.	1-6
Jalapin	"	1-67	" " jalap	m.	1-22
Juglandin	"	1-6	" " juglans	m.	2
Koussein	"	1-6	" " kousso	m.	3
Leptandrin	"	1-6	" " leptandra	m.	3
Lobelin	"	1-12	" " lobelia	m.	1-3
Lycopin	"	1-6	" " lycopus	m.	5
Macrotin	"	1-6	" " cimicifuga	m.	2 1-2
Menispermin	"	1-6	" " menispermum	m.	5
Morphine sulph	"	1-12	" tinct. opium	m.	3
Myricin	"	1-6	" " myrica cerifera	m.	5
Narceine	"	1-67	" tinct. opium	m.	1-3
Nickel bromide	"	1-6	" potass. bromide	gr.	2
Physostigmine	"	1-1000	" fl. ext. physostigma	m.	1-5
Phytolaccin	"	1-6	" " phytolacca root	m.	1-3
Picrotoxin	"	1-134	" " cocculus indicus	m.	5
Pilocarpine	"	1-67	" " pilocarpus jaborandi	m.	2
Piperine	"	1-6	" " piper nigrum	m.	2
Podophyllin	"	1-12	" " podophyllum	m.	1
Podophyllotoxin	"	1-12	" " podophyllum	m.	12
Populin	"	1-6	" " poplar	m.	2 1-2
Quassin	"	1-67	" " quassia	m.	5
Quinine sulph.	"	1-6	" " cinchona calisaya	m.	5
Rhein	"	1-6	" " rhubarb	m.	1
Rumicin	"	1-6	" " rumex crispus	m.	2 1-2
Salicin	"	1-6	" " salix nigra	m.	2 1-2
Sanguinarine	"	1-67	" " sanguinaria	m.	1
Scillitin	"	1-67	" " scilla mar.	m.	1-6
Scutellarin	"	1-6	" " scutellaria	m.	7
Senecin	"	1-6	" " senecio	m.	2
Solanine	"	1-67	" " solanum Carolin	m.	1-2
Sparteine	"	1-6	" " scoparius	m.	30
Stillingin	"	1-6	" " stillingia	m.	1
Strophanthin	"	1-134	" tinct. strophanthus	m.	14
Strychnine	"	1-67	" " nux vomica	m.	10
Veratrine	"	1-134	" " veratrum vir.	m.	3
Verbenin	"	1-6	" " verbena	m.	2 1-2
Viburnin	"	1-6	" " viburnum prunifol.	m.	1
Xanthoxylin	"	1-6	" " xanthoxylum	m.	5

CHAPTER VI

The Synergism of Drugs

We who especially study the action of definite active principles believe that the bulk of our clinical work should be done with single remedies, each administered with a distinct object. The action of a single remedy may be watched and estimated more readily, and we learn better how much it requires to produce a desired effect, how long it takes and when to stop it. Disease, as clinically presented, may be rarely so simple as to present but a solitary indication, and several drugs may require attention at the same time; but it is certain that with each addition the task of watching the effects is increased—and how any man can carry on a dozen different remedial operations at the same time, we leave to the phenomenon who plays many games of chess at once.

Only after one has had long experience in the administration of single remedies should he commence to combine them. But he then may be qualified to do this and with results never dreamed of under the old system of prescription building. Under the latter we combine several remedies, each of which may suit the case, in the hope that some one of them shall do so; or we give the indicated remedy and throw in one or more adjuvants to get more effect. The very pertinent question of why not give a larger dose of the principal ingredient, is unanswerable.

In several instances it has been noted that the union of a number of agents acting on the same general system seems to exert a greater power than any one of the ingredients in a dose equivalent to the combination. For instance, if we combine three cathartics, each of which exerts alone an action that may be designated schematically as one, the combined effect, instead of being three, may equal six or more. How can we explain this singular observation?

Suppose we desire to increase the elimination through the skin —we may do this by stimulating the activity of the sudoriparous glands or by relaxing the tension of the cutaneous vessels. If we administer a secretion stimulant and at the same time remove an obstacle to its action by relaxing the vasomotors, we get from the secretion stimulant a decided effect, whereas we may have had little if any effect from either of the remedies if administered alone in the same dose.

Years ago Brunton called attention to the fact that if we add a very minute dose of atropine, or of morphine, to our purgatives, we increase their purgative effect, by paralyzing the inhibitory

nerves that constitute an obstacle to the purgative action. If the dose of atropine is increased we get a sedative action on the intestinal musculature, which interferes with the purgative action instead. Given alone, the minute dose of atropine would not purge at all. Given with true purgatives the latter act in smaller doses than if the atropine were omitted.

Arbutin is an ideal remedy for irritations of the bladder. Such irritations may be increased or even aroused by the presence of oxalates in the urine. We know that such catarrhal affections once set in operation do not necessarily stop when the original excitant is removed, any more than does an epilepsy. But if the oxaluria is stopped by a little nitric acid before meals, or by treatment of duodenal fermentation, the urinary irritation will subside under smaller doses of arbutin and more speedily than it will if the oxaluria is neglected.

Heart weakness is an exceedingly complex matter, taking in as it does the condition of the muscular and nervous elements of the heart and the blood-vessels, the central nervous system, and the quality of the blood itself, etc., and possibly on the therapeutic studies of the next generation we may base a discriminating choice among the heart tonics. But many prescribers have affirmed that they get a better effect from a combination of several heart-tonics in minute doses than from a comparatively equivalent dose of any one of them. It may be, as is assumed, that each of these tonics acting on a different mechanism or function, we have a general, uniform increase of tone of the entire apparatus, better than an inordinate and unsustained toning of a single part or function, the others not being coordinately strengthened. This at least expresses the clinical observations made—whether it be literally true remains to be demonstrated. Meanwhile it is simply an excuse for the old empiric style of prescribing, but points to a desirable path for investigation.

A similar hypothesis may be formulated to account for a phenomenon recognized in studying the effects of the hyoscine-morphine-cactin compound anesthetic. Much of the anesthetic effect is due to the depression of cutaneous sensibility both by hyoscine and morphine; but it seems that the effect of the combination notably exceeds that of either ingredient when administered alone. Assume that the cutaneous anesthesia due to morphine, gr. 1-4, equals schematically ten, and that of hyoscine hydrobromide, gr. 1-100, equals twenty, the effect of the combination seems to be nearer sixty than thirty. These figures are of course simply

assumed, as an effort to explain hypothetically a phenomenon witnessed in the clinical field; and they should be tested by experiment before acceptation.

But it is not difficult to explain such an observation. The cutaneous sensibility may be directly reduced by one agent and the conductivity of the nerve-trunks by the other; so that no sensation at all is transmitted, whereas even with a much larger dose of the one agent or the other some sensation would pass to the brain. That is, we assume that we may by the one reduce the cutaneous sensibility to one-half the normal; doubling the dose will not entirely abolish the remainder. By the other we may similarly reduce the transmitting power of the nerve-trunks, and double the dose will not entirely abolish this function. But if we at the same time reduce to one-half the nerve-sensibility of the skin, and the transmitting power of the cords, the latter will not be able to transmit any of the enfeebled impression on the cutaneous nerve endings.

We are conscious that this explanation is not satisfactory and are ready to hear it questioned; also to listen to any better explanation of the phenomenon that may be offered.

This brings up another, though a tangential, observation as to the action of this hyoscine, morphine and cactin combination: the anesthetic action seems to be directed in large part against the cutaneous sensibility rather than against the cerebral centers. A physician recently took one of the tablets in our office and one hour later entered the office of a down-town dentist, where he had a sensitive nerve-pulp removed from a tooth, without pain. During, as before and after, his visit with the dentist, he transacted his business without impediment, the effect on the consciousness being trifling. If we can develop an anesthetic that acts as such solely or largely on the peripheral tissues involved in operations, and least on the cerebrum, it is surely an advantage and a development in precise application of remedies. Many observations have been made that harmonize with this one, and the matter seems worthy of study and development.

CHAPTER VII

Prescriptions

The greatest enemy to scientific therapeutics today, as ever, is the habit of using combinations of remedies to meet single indications. The usual method of combining remedies, when the physician does not copy a formula entire, is about like this: Having to

treat a cystitis, the doctor recollects that uva ursi, pipsissewa, pareira brava and buchu have been found useful in this affection, so he orders an ounce of each of their fluid extracts; dose, a teaspoonful every four hours. If the patient improves this becomes his standard prescription for cystitis. As to the action of each he never has a glimmering of an idea. By and by he hears triticum recommended for such cases, and he adds to the formula an ounce of its extract. If the effect seems better the triticum henceforth forms a constituent of his prescription.

In the meantime the druggist runs out of one or more of these ingredients, or finds them more costly than the rest, so he leaves them out and fills the bottle up with the cheaper ingredients or with old stock he wants to get rid of. Or, learning that the patient's bladder is irritable he slips in a little hyoscyamus and an alkali, well knowing that the doctor will never suspect the alterations or notice the difference, unless it is to attribute the superior efficacy of the remedy to the druggist's better quality of drugs.

The active principle practician goes to work differently: Finding in all the popular remedies for cystitis one active principle, arbutin, he employs that alone; and pushes the dose till the effect is manifested. No substitution escapes him, for he knows just what effect to look for, and he looks for it. If the bladder is very irritable he adds hyoscyamine to get quick relief. If the urine is too acid he adds an alkali. For every addition he has a reason, and expects a definite result. If this does not follow he knows there is a reason, and this he searches in the conditions of the case and the quality of his remedies.

In truly scientific prescription building every remedy is employed with a distinct object. From it a definite result is expected, which is looked for; and if it fails to appear, the reason is sought. The prescription is consequently made at the bedside, and is aimed at the conditions then and there presented by that particular case. It is a poor sort of a doctor who does not find reason to alter the form or the administration of his prescription at each visit, in acute maladies.

For these reasons the use of single remedies for single indications is the rule, and compound remedies are discountenanced, with a few exceptions. These few relate to combinations that have won such a place in professional favor that they are employed as therapeutic entities, regardless of their individual components. The type of this class is Dover's powder. With others, a very few, the combination fits pathologic complexes occurring so frequently that

convenience allows the application of the combination with like frequency. The best examples of this class are the Dosimetric Triad of Burggraeve, and Abbott's Defervescent Compound. In these the basal ingredients are aconitine and digitalin. The former relaxes vascular tension, the latter increases it. It was a stroke of Burggraeve's genius that he recognized that, in every febrile malady involving an alteration in the circulatory equilibrium, some blood accumulated in part of the circulatory area—vascular paresis—while it was wanting from other areas—vascular spasm. The great clinician drew the inference that the two antagonistic remedies might be administered simultaneously, and each would act on that part where its special action was needed to restore normal equilibrium. To the basal couple Burggraeve added strychnine arsenate, inciting the vital functions and furthering resolution; while for the sthenic forms common in America Abbott added veratrine, moderating excessive heart-action and stimulating elimination. The disturbance of circulatory equilibrium is so frequently to be recognized, in non-febrile as well as in febrile maladies, that these combinations are constantly required in our every-day practice. But as yet the list is scarcely to be increased, and it is much to be preferred that the physician form the habit of making his own combinations whenever more than one remedy is needed. Every addition makes it more difficult to watch the effects and to distinguish them from the natural course of the malady.

The study of the active principles has served to direct attention to the fact that these definite remedies are to be directed against pathologic conditions rather than diseases. There are no specifics for various diseases, but many readjusters of disorders of vital function, which may be present in many diseases.

Arsenic favors fatty degeneration, and may be aimed against the forming but as yet unorganized exudates and debris of any malady. It also, as is now believed, imparts to the red blood corpuscles an increased resistance against attacking microorganisms of any description. Nuclein multiplies and activates the leukocytes, hence is of untold value in all infectious diseases. Berberine imparts tonicity to relaxed connective tissue; boldine increases the hepatic product of urea, etc.

But there is in truth not a solitary specific known for any single named disease. Quinine will not cure all cases of malaria, antitoxin all cases of diphtheria, mercury or "606" all of syphilis, pilocarpine all of erysipelas; possibly the sulphides may not cure all cases of gonorrheal infection, but as to this we cannot as yet speak with certainty.

The use of active principles therefore will never make of medicine an easy, nickel-in-the-slot system; but on the contrary it drives the physician back to the sick-room, where, in the laboratory of nature, he studies her operations as displayed in the individual patient. After availing himself to the fullest of all the aids offered by modern science, by the laboratory, he must yet complete his work by acute, intelligent, trained clinical observation—and therapeutics.

CHAPTER VIII

Classification

In the older works on therapeutics some attempt was made to simplify the labors of the student by grouping the remedies into classes. No system of classification seemed absolute, and of late writers have given up the task and contented themselves with an alphabetic arrangement. This is convenient for the man who has already learned to classify remedies but vastly increases the burden thrown on the beginner's memory. It is hence objectionable in a textbook for medical colleges, but possibly answers in a work designed for the practician.

Sollmann gives no formal classification but treats of drug remedies, in groups, as follows: Convulsant series—strychnine, caffeine, and picrotoxin groups. Alkaloidal hypnotics—morphine, cannabis and hydrastine groups. Cocaine and its substitutes. Atropine group. Muscarine series. Internal secretions. Apomorphine, aconite, quinine, coal-tar, toxin and antitoxin, hydrocarbon narcotic, gases, camphor, cyanide, nitrite, digitalis, ergot, sapotoxin, cough remedies, osmotic, cathartic, diuretic, and other groups.

Kobert treats of remedies under the following heads:

First part: Pharmacotherapeutic remedies, whose effect is not limited to one organ.

1. Immunizing remedies.
2. Caustic remedies.
3. Hemostatic remedies.
4. Cicatrix-softening remedies.
5. Membrane formers.
6. Derivatives and antiphlogistics.
7. Antimicrobic remedies. (*a*) Disinfectants of unliving substances. (*b*) Remedies against pus. (*c*) Remedies against microbes in bodily cavities.

8. Antituberculosa and antiscrofulosa.

9. Antisyphilitica.

10 Antifebriles.

11. Antidyscrasics. (*a*) Antidiabetica. (*b*) Antifats. (*c*) Antiarthritica.

Second part: Pharmacotherapeutic remedies whose effects are limited to a certain organ or to a certain system of organs.

1. Organotherapeutica.

2. Remedies whose effects extend to the compact substance of the bones.

3. Remedies whose effects extend to the blood and to the blood-making organs. (*a*) Remedies whose effects extend to the blood plasma. (*b*) Remedies whose effects extend to the white corpuscles, referring also to their place of formation. (*c*) Remedies whose effects extend to the red corpuscles and their place of formation.

a. Remedies against poisons which change the hemoglobin into useless combinations.

b. Remedies against poisons or diseases which dissolve the red corpuscles or which destroy them deeply.

c. Remedies which come to be considered in insufficient formation of hemoglobin, and red corpuscles; viz.: Antichlorotica.

4. Remedies whose effects have reference to the vascular system and the heart. (*a*) Remedies which increase the blood-pressure and the rapidity of the circulation. (*b*) Remedies which depress the pressure and the rapidity of circulation.

5. Stimulants of cerebral activity.

6. Diuretics.

7. Skin remedies: (*a*) Sudorifics. (*b*) Antisudorifics. (*c*) Skin irritants. (*d*) Local skin anesthetics. (*e*) Remedies against animal parasites. (*f*) Remedies against other cutaneous diseases.

8. Narcotics. (*a*) Inhaling anesthetics. (*b*) Narcotics against pain and sleeplessness.

9. Nervina.

10. Mouth remedies.

11. Stomachics and digestives.

12. Emetics.

13. Antiemetics.

14. Cathartics.

15. Anthelmintics. (*a*) Against tapeworm and anchylostomata. (*b*) Against ascaris lumbricoides.

16. Antidiarrheica.

17. Remedies in the diseases of the respiratory organs.

18. Galactagogs.

19. Remedies affecting the genital organs. (*a*) Aphrodisiaca. (*b*) Antaphrodisiaca. (*c*) Ovarina. (*d*) Uterina. (*e*) Remedies against venereal disease: (1) Against venereal papilloma. (2) Against non-syphilitic buboes. (3) Against the ulcus molle (soft chancre). (4) Against gonorrhea. (*f*) Remedies against enuresis nocturna. (*g*) Remedies against albuminuria.

20. Eye remedies.

Third part: Antidota.

1. Physical mechanical treatment.

2. Pharmacological treatment.

a. Group of remedies to envelop the poison.

b. Group of remedies which destroy the poison by oxidation.

c. Group of chemical antidotes

d. Group of socalled physiologic antidotes.

Burggraeve made the following classification: 1. Defervescents: aconitine, veratrine, salicylic acid. 2. Vital excitants: strychnine and brucine. 3. Antiperiodics: quinine and arsenic. 4. Sedatives, subdivided into (*a*) narcotics: codeine, hyoscyamine, cicutine; (*b*) antineurotics: the valerianates and camphor monobromide; (*c*) analgesics: chloroform, iodoform, cocaine. 5. Eliminants, subdivided into (*a*) expectorants: emetine and apomorphine; (*b*) sudorific: pilocarpine; (*c*) diuretics: digitalis, asparagin, scillitin, caffeine; (*d*) purgatives: podophyllin, bryonin, colocynthin, saline laxative. 6. Digestive tonics: for the stomach, quassin; for the intestines, jalapin. 7. Reconstituents: arsenic, iron, iodine and their salts. 8. Antimicrobics: phenol, salicylic acid. 9. Vermifuges: santonin, pelletierine, kousseine.

To these Laura adds the elective modifiers, constitutional or organic: the mercurials, iodides, caffeine, digitalis, etc.

Butler divides remedies into two classes: first, those used in cases which cannot be relieved by a single dose, but require repeated and long administration; second, those employed in cases for immediate relief by the exhibition of a single dose. Those of the first class he terms disease or organic remedies, to act upon the point of departure of physiologic action in the living organism. Those in the second class are employed for the relief of such manifestations as pain or other disorder in the system, and are therefore termed system or functional remedies. The administration of these remedies is usually for the cure of chronic diseases and prevention of complication in acute diseases. These medicines are

further divided into restoratives, alteratives and antiseptics. Under restoratives he ranks fats and oils, mineral acids, organic acids, alkalies, mineral waters, simple and aromatic bitters, hematics and animal extracts. Under alteratives he ranks remedies that act only as such in diseased conditions. With these he speaks of serums. Among systemic medicines he makes the following groups: Antispasmodics, antipyretics, anesthetics, hypnotics, narcotics, motor excitants, motor depressants, cardiac stimulants, cardiac sedatives, diaphoretics, expectorants, diuretics, hematics, emmenagogs.

CHAPTER IX

Dosage

The ancient idea of stimulation was that the more of the stimulant given the greater its stimulus. Whisky was looked upon as the ideal stimulant, and if a physician allowed a patient to die of debility, it was simply because he did not give whisky enough. This crude conception of the action of remedies has long since passed away. Our ideal of remedial action now is analogous to the regulation of a watch. We seek to elevate the depressed function or moderate an exaggerated one, until we reach exact physiologic equilibrium.

For this purpose, following Burggraeve's method, we give minute doses of the indicated remedy, repeated at intervals whose rapidity is determined by the solubility of the drug and the time it requires in getting into action. These small doses are continued until we get exactly the effect we desire. Very often the drug is to be continued until some evidence of its action is manifested. As this evidence of action is usually an exaggeration of one or other of the vital functions, we may put it down as a general rule that evident action is toxic action. Hence when such action is manifest, if the malady is one in which the continued effect of the drug is desirable we moderate the dose to just below that of inducing manifest action, and continue it for such a period as may be desirable.

A good illustration of this is the action of mercury in the treatment of syphilis. Here we have a direct toxic action to be exerted on the living element of the disease, and it is obvious that we should obtain the greatest possible action from our drug and that as quickly as possible. We therefore administer the small dose continuously until the beginning of toxic action is shown, by the effect of mercury

upon the mouth, or that of the iodides of mercury and arsenic upon the eyelids; then reduce until these toxic manifestations cease, when the drug is continued as long as the case requires. This dose, that is, one which is just below that which induces manifest toxic action, is known as the physiologic dose, and in the majority of instances this is the curative dose. When we desire to combat an invading micro-organism by the use of calcium sulphide, the same rule holds good. In fact it may be taken as the general rule in the administration of medicine, with some exceptions.

For instance, in the treatment of epilepsy with solanine, we are guided by the appearance of the paroxysms, and we continue to increase our doses of solanine until the paroxysms no longer recur. This may require at first much larger doses than the physiologic, and these must be continued until the effect of the convulsive habit is overcome.

The researches of Dr. T. G. Mays and others indicate that in all probability all remedies are stimulant in small and sedative in sufficiently large doses. In the therapeutic application of all remedies it is therefore absolutely essential that the physician should distinguish between small-dose and large-dose effects.

Without this explanation the contradictory verdicts of various observers as to the action of many remedies are absolutely inexplicable; with it the matter is quite simple. Take anemonin for instance: we find some observers assert that this drug and its parent plant, pulsatilla, are valuable remedies in a certain line of diseases, and there is general unanimity as to the nature of the affections to which it is applicable, and as to the curative results secured. Others on the contrary state that the drug is practically worthless. We find, however, that all those who pronounce a favorable opinion on this drug use it in very small doses, and those who discard it tried it in quite large doses. The difference is obvious.

By this method of rapidly repeated doses we avoid at the same time almost all the disadvantages accruing from the medium or maximum doses. Idiosyncrasy is wholly provided for by this method, and the differences relating to sex, weight, temperament, the presence or absence of disease, in fact all those influences which modify the effects of remedies and make the doses required to produce a desired result vary over a wide range, are all swept away, needing no further consideration.

In the case of children it is usual, in administering the powerful alkaloids, to follow the rule made by Prof. John M. Shaller: Take one granule of the remedy for each year of the child's age, add one

more granule, put these in a glass with twenty-four teaspoonfuls of water. When dissolved, one teaspoonful of this should be given at the usual intervals, as required by the average adult, and the remedy continued until the desired effects have been obtained.

In cases of emergency with either adults or children much larger doses may be given, especially when we have used this remedy on the same patient previously and are aware of what his reaction will be. Most of the alkaloidal granules are made up with pure sugar of milk, are quite soluble, and may be employed hypodermically. This cannot be done with the resins, which are not soluble in water.

Prof. J. H. Salisbury called attention to the fact that when remedies are absorbed from the mouth they pass directly into the general circulation and exert a quicker and more powerful action than when taken into the stomach, whence they are absorbed into the gastric and intestinal veins and carried to the liver. This organ intercepts the alkaloids and throws them out into the alimentary canal for excretion. The effect exerted by these agents is due to the proportion of the dose which escapes this action of the liver and enters the general circulation. To obtain the fullest action from the smallest quantity of the remedy, it is well to hold it in the mouth as long as possible, that it may be absorbed thence directly into the circulation.

In practice we have not found the difference as great as Prof. Salisbury suggests; still, there is a difference, enough to warrant careful consideration.

To physicians with time at their disposal and the possession or control of land, we would recommend the consideration of drug farming and the extraction of alkaloids as a pleasant occupation for a side line. Probably the best results would be secured were each to select a single plant and devote his attention to it. Select that plant which is best suited to the soil and climate in your location; next, experiment with the idea of ascertaining how it may be best grown so as to yield the largest proportion of the active principle. Then obtain the necessary apparatus and make of yourself a special producer of this alkaloid. This is much more worthy of the physician than devising a patent combination and advertising it. In Germany certain individuals do this, and one man may produce all of the alkaloid which is sold by the great manufacturing houses.

There is no reason why such work should not be done in America, if taken up scientifically by those who are qualified to perform such work, or those who are able to make themselves qualified.

PART II

THE ARMAMENTARIUM

ACETANILID

Acetanilid is soluble in 194 parts of cold water, 2.50 (Merck) at 77° F. of alcohol, 18 of boiling water, 12 (Merck) at 77° F. of ether, freely in chloroform, and in 0.4 of boiling alcohol. It is sedative to the stomach, and allays nausea. Small doses have no effect on the constituents of the blood, but large ones destroy the corpuscles; the arterial blood becomes venous, its alkalinity is decreased, the hemoglobin reduced to methemoglobin. Ordinary doses raise vascular tension slightly, slowing the heart, while toxic doses depress the heart and the vasomotors, relaxing vascular tension. Small doses mildly stimulate the brain, larger ones sedating the sensory nerves and the cord. Toxic doses cause general anesthesia, abolish the reflexes, and paralyze the motor and sensory nerves. No effect is exerted on the respiration by any short of toxic doses, which cause rapid, labored breathing. Death is due to asphyxia; direct, from action on the center, and indirect from paralysis of the peripheral motor nerves and destruction of the oxygen-carrying power of the blood.

Acetanilid is an active diuretic, increasing the excretion of urea and of uric acid, toxic doses causing hemoglobinuria. It is also diaphoretic. It is excreted by the kidneys as para-amido-phenol sulphate. On normal temperatures it has no effect but exerts a very marked antipyretic action on febrile heat. This is attributed to a direct action on the heat center. Toxic doses contract the pupil. The prolonged use of this agent induces congestion of the kidneys, liver and spleen. Sneezing, somnolence, redness, chilliness and cyanosis are occasional effects of ordinary doses. When toxic doses are taken cyanosis appears, the face livid and anxious, skin covered with cold sweat, pulse soft, slow and weak, with profound prostration, sometimes vomiting. Respiration is at first fast and laboring, getting slow and shallow, death resulting from respiratory paralysis. Autopsy shows the heart, liver and kidneys in a state of fatty de-

generation. The treatment of poisoning is by diffusible stimulants; coffee; atropine and strychnine hypodermatically; external heat, and oxygen inhalations (Butler).

Although acetanilid is not employed nearly so recklessly as formerly, and it has been laid aside by many practicians, there are times when it is a useful resource, from its unquestioned power in acute, high, sthenic fever, where prompt and powerful action is indicated. Here it may be given in doses not exceeding two grains, repeated every one or two hours, carefully watched lest collapse ensue. The very high fevers of the early stages of the exanthemata are examples. Hyperpyrexia in any disease may require acetanilid if the cold bath is not available. In rheumatism it may be employed until the temperature falls below 105° F. Butler here limits the safe dosage to 18 grains *per diem.*

Acetanilid possesses remarkable virtues as an analgesic, the painful crises of locomotor ataxia yielding to it, as well as the pains of other spinal maladies, all neuralgias, neuritis, lumbago, gastralgia, dysmenorrhea, sciatica, and most headaches. Ignorance of the disastrous effects of the continuous use of this remedy has led to its employment to a perilous extent by the laity. For its uses as an analgesic acetanilid should be employed in connection with other remedies, such as caffeine to guard against cardiac depression, ammonium bromide to increase the cerebral analgesia, sodium salicylate as an antirheumatic and antiferment, etc.

Butler further enumerates uses of acetanilid for chorea and diurnal epilepsy, with full habit and high vascular tension, paroxysmal pains in general, the excitement of *mania a potu*, the paroxysms of whooping-cough, seasickness, traumatic tetanus, acute bronchitis and influenza—here also in the combinations suggested above. He considers it contraindicated in low fevers, fatty or dilated heart, blood disorders, advanced tuberculosis and exhaustion from hemorrhages. Shoemaker says toxic symptoms are especially apt to occur if the acetanilid is impure, acetotoluid being present. He speaks of its use to break the paroxysms of asthma, for the dysmenorrhea of young girls, and for obstinate nervous vomiting.

ACONITINE

Standard granules—Aconitine (Abbott), alk., gr. 1-134, Gm. .0005.

Aconitine was discovered by Geiger and Hesse in 1833. It occurs in crystalline and in granular form. It is permanent in the air, odorless, the taste bitter at first, then sharp and tingling. When

yellow it is impure and the taste is more burning. It is soluble in alcohol, ether, chloroform and hot water. It is absorbed through the healthy skin from chloroform solution; or from wounds, ulcers or abrasions. For hypodermic use the nitrate is best, being quite soluble in water. The injections are very painful. Aconitine is found in Aconitum napellus, ferox, japonicum, and many other species, five of which are found in America.

Merck gives the formula as C_{33} H_{45} N O_{12}.

Duquesnel's method of extraction is as follows: 100 parts of powdered aconite root are mixed with one part of tartaric acid; this is exhausted by repeated percolation with cold alcohol, and the liquid evaporated at a low temperature on a water bath to the consistence of a fluid extract. To this is added distilled water, and the precipitated resinous and oily matter removed by filtration. The resultant solution of aconitine tartrate is then precipitated with a slight excess of potassium bicarbonate, agitated with washed ether and the two fluids separated with the siphon. The ethereal solution is shaken four or five times with a ten-percent solution of hydrochloric acid, which takes up the alkaloid from the ethereal solution. The acid liquids are treated with calcium carbonate to saturation, to prevent the acid injuring the aconitine; the mixture is evaporated at a very gentle heat, filtered, and while still warm mixed with a solution of sodium nitrate (2 of salt to 3 of water), having the same temperature. The whole is allowed to cool slowly during several hours and set away for several days' rest, when the crystals separate out as a crust on the bottom.

Laura opens his discussion of aconitine with an emphatic and reiterated protest against the use of aconite, and of the nondosimetric or spurious aconitines; and also against the use of massive doses of true aconitine. The false alkaloids, he believes, contain an exceedingly toxic acrid principle to which their poisonous properties may be ascribed. He pronounces the English aconitine ten times more toxic than the German, while the Hottot aconitine is five times more toxic than the English.

To obtain the results that justify the dosimetrist in placing aconitine at the head of all drugs, it must invariably be administered in small doses at regular intervals, proportional to the idiosyncrasy of the patient and the nature, the violence, the obstinacy and the resistance of the disease; besides, all medicaments must be chemically pure. Dosimetric therapy rests on these two rules.

Before Burggraeve's day Husemann spoke of the difficulty of distinguishing between the related species of aconite gathered in the

Alps, whose mixture formed the product found in pharmacies, and added: "This confusion of species readily explains the results following its use in ignorant hands." The root gathered before the plant blooms is infinitely more active than that gathered in autumn. The strength varies with the Alpine origin of the plant; and Schroff found the cultivated variety less active than the wild.

Gaue and Webster (Merck's Report, June 1910, p. 165), say that the aconitines of commerce are variable owing to difficulty in obtaining it pure. They suggest the use of the crystalline hydrochloride or hydrobromide instead, which are more soluble, more easily purified and therefore more uniform.

The remedial and the toxic principles are present in varying proportions; all of which, Laura ironically observes, shows how uniform and certain are the pharmacopeial preparations of aconite!

In some species the flowers and leaves are inert, the roots very poisonous; others depend on the place where they are grown, as one variety is very toxic in the north of India but harmless in other provinces, where it is used as a food. The Lapps sustain life on the wolfbane, aconitum lycoctonum, whose roots equal in toxic energy those of aconitum ferox and surpass in violence all other species.

Besides aconitine and the acrid toxin, aconite contains several active principles, ill defined, which produce effects other than those of aconitine and in so far modify its action to an unknown degree and in an unknown manner. A few drops of the tincture have induced poisoning. (Skinner.) Pereira reported accidents following one milligram of English aconitine, such as have never followed the pure dosimetric granules, used every day by thousands of physicians and at both extremes of life. Schroff declares that while there is identity of action in some respects between aconitine and the extract of aconite, in other respects their action is altogether different. The galenics he found to cause a very intense phlogosis of the digestive apparatus, inducing eructations, heartburn and vomiting, none of which follows pure aconitine, any more than does the very extensive and typical formication described by Cantani. These Laura attributes exclusively to the acrid toxin found in the galenics.

"The discovery of this principle was a notable event. Not only was the physician thereby delivered from the inconveniences, the uncertainties and the perils of the ordinary pharmaceutic preparations, but he was also freed from the uneasiness and the errors resulting from the administration of aconite, of which reports by its partisans were so contradictory, making these preparations

appear uncertain, unstable, readily alterable, and giving a picture of the most humiliating anarchy. Dosimetry, bringing art out of chaos, has restored us to the right road.

"That which especially renders the rule of small and oft-repeated doses imperative is the resistance of the human organism when in the state of illness. Disease arouses such a resistance. While all remedies put in rapport with the human organism under all circumstances act in the same manner and develop their particular activities, it is no less certain that this action is manifested by results differing as they operate upon a healthy organism or a diseased one, in the latter case restoring an equilibrium that normally exists already in the former.

"Experiments on animals and on healthy men have their value, but the action of medicaments can only be determined in a scientific and certain manner by clinical observation and experiment. The remedial application of drugs finds its only sure foundation in their therapeutic administration. In sickness new conditions are presented that necessarily vitiate conclusions drawn from experiments made under others. Agents surely injurious to the well man may solace the sick, doses perilous to the former may cure the latter.

"Never forget that sickness modifies our general susceptibility to hygienic and moral agencies, and vastly more yet to drugs. The most dangerous may be tolerated remarkably, the feebler may demonstrate an exaggerated impressibility. So children may bear large doses of quinine, and hysterics may be acted upon violently by the smallest doses; while twenty or more granules of aconitine given singly to a healthy man may manifestly depress the cardiopulmonary centers, etc., the same or larger doses are well tolerated by an organism wasting with fever, and this the more as the fever is higher. Whatever may be the origin or the nature of the fever which aconitine is called upon to vanquish or to moderate, its sedating action on the great organic systems is considerable and sure, it serves as a counterpoise to the morbid exaltation of the great nervous and circulatory factors which it restores to equilibrium.

"Furthermore, dosimetry, with its fractional and successive doses, notes and measures the effects of its agents and never permits them to cause accidents such as too often follow the ordinary therapeutics. The dosimetrist allows himself to be guided by his clinical observations in the choice of remedies and in their dosage. We repudiate an absolute posology, abstract and determined *a priori*, as a veritable absurdity, physiologic and therapeutic, and we claim as a necessity that every morbid condition must be treated

by means appropriate and adapted to each condition itself; that the remedy must be given with a precise object, calculated in advance, according with the patient and the disease, to secure the desired physiotherapeutic effect. Without this, one makes a false passage and misses the cure or obtains it only imperfectly and late—the patient suffers, the physician wins little credit, the dignity of our art is wounded.

"For example: The physician called to treat a pyrexia finds the indication for aconitine—*nature* of medicament. He cogitates the method of administration—*dose* of medicament; this is determined according to the activity, the violence, the intensity of the febrile process, together with other considerations derived from the nature of the malady, its localization, complications, the danger to the existence or the function of an organ, an apparatus, a partial system of the general economy, the particularities resulting from age, sex, constitution, idiosyncrasy, morbid antecedents of the patient, and so forth.

"The action of aconitine thus employed is sedative and moderating. When chewed or swallowed with but little water, it causes a sense of tingling in the tongue and palate, with more or less constriction of the isthmus and pharynx—symptoms not present when the granules are swallowed whole or dissolved in larger quantities of water or milk. To adults, to the aged, and to large children give the granules dissolved in a little water; to very young children give in an exactly measured quantity of milk.

"Aconitine exercises a very efficacious sedation over the vasomotor centers. With healthy men small doses often act as cardiovascular excitants, an action slight, evanescent, quickly subdued by antagonistic remedies; the temperature is yet depressed persistently, the pulse softened and slowed, respiration rendered easier and deeper, diuresis and diaphoresis are favored, and calm, tranquil slumber is induced. The fall of temperature keeps pace with the relaxation of arterial tension. Toxic doses paralyze the respiration and then the heart.

"Aconitine, that calmant *par excellence* and most active regulator of the great cerebral and circulatory centers, is also the most powerful antipyretic, and should be preferred in the treatment of febrile phenomena, essential or symptomatic, over those agents termed antithermics, from the promptness, sureness and duration of its action, the simplicity of its administration and the facility with which all patients take the granules, an advantage accruing to the entire dosimetric therapeutics."

Van Renterghem gives the following as the total dose of several aconitines inducing the first evidences of toxic effect; taken within twelve hours.

Duquesnel's .....gr. 1-20
Merck's crystallized .....gr. 1-22 to 1-17
Merck's amorphous .....gr. 1
Chanteaud's granules .....gr. 5-6
Friedlaender's .....gr. 15

Merck gives the following single dosage:

Aconitin (eclectic resinoid) 0.003—0.005. Aconitine pure, crystal,0.0001—0.00035; single maximum 0.0001, daily 0.003. Aconitine, pure amorph., 0.001. Aconitine from A. Ferox, 0.00026—0.00065.

The arsenate, hydrobromate, hydrochlorate, nitrate, phosphate, salicylate and sulphate are listed; doses same as of the alkaloid.

Van Renterghem found after rinsing the mouth and then taking into it a solution of aconitine that the activity of the drug could be noted locally in from a few seconds up to ten minutes. Sometimes the effect was manifested upon the tongue, at other times upon the palate. The first subjective symptoms independent of the local action presented themselves after twelve to forty-five minutes.

Hottot found that after taking a dose of aconitine the local symptoms developed in the mouth and throat almost immediately. The symptoms following a full dose endured from ten to sixteen hours, then subsided gradually, and the next day there was still dryness of the throat and heaviness of the head, with extreme lassitude.

Burggraeve found an ordinary dose followed in a few seconds by local symptoms, quickly followed by the general ones.

One granule of aconitine (Abbott), gr. 1-134, approximately equals 2.8 m. of a standard, full-strength tincture of aconite.

Physiologic and Toxic Actions.—1. The sensory nerve-ends are first stimulated, with tingling, warmth, sneezing, salivation, coughing, vomiting, neuralgic pain; later comes paralysis of tactile, temperature, pain and special sensation. The fifth cranial nerve is especially affected, the tongue, lips and cheeks; the other nerves in the order of their sensibility, those of the face, perineum, breast, belly and lastly the back.

2. The motor nerves are probably unaffected, as well as the muscles; the fibrillary twitching being possibly due to irritation of the intramuscular nerve-ends. The weakness may be attributed to the feeble circulation and innutrition. When applied directly, aconitine abolishes the irritability of all nerve-fiber.

3 The vasomotor medullary center is first stimulated and then depressed; the nerves and ends are unaffected. Arterial tension is lowered, the vessels containing less blood, the pulse becoming soft and dicrotic.

4. The mental faculties are not directly affected, but may become clouded by carbonic acid poisoning.

5. The vagus inhibitory center is strongly stimulated, slowing the heart and prolonging the diastole, the work done by each systole is notably increased, the auricles continuing to beat after the ventricles have ceased, their rhythm becoming disassociated. In lethal doses the stimulation of the intracardiac inhibitory apparatus may exceed or outlast the stimulation of the center, and the heart beats strongly, rapidly and irregularly, passing suddenly into "cardiac delirium."

6. The respiratory center is directly depressed, breathing is slowed, expiration labored, the accessory muscles being called into prominent use; dyspnea occurs, the respirations become shallow, and death occurs by asphyxia. Convulsions may precede death.

7. The temperature falls, either from the normal or in fever. The fall is increased by cold, retarded by heat. This effect may be due in part to a direct effect upon the heat-regulating center.

8. The saliva is increased by direct irritation; the perspiration as a symptom of depression. Other secretions are increased doubtfully. Gastrointestinal irritation is a local effect.

9. Oxidation is unaffected.

10. The pupils are first contracted, then dilated widely.

11. Aconitine is rapidly absorbed by the tissues, disappearing from the blood. It is excreted by the kidneys, traces appearing in the bile and saliva.

Atropine antagonizes the vagus inhibition and by sustaining respiration may save life when a lethal dose has been taken. But if the dose of aconitine be sufficiently large, death will still occur from heart-paralysis.

In physiologic doses aconitine relaxes and slows the pulse and respiration, lowers the temperature and the vascular tension, equalizing the circulation and dissipating hyperemia.

In toxic doses it causes tingling of the skin followed by anesthesia, salivation, slow labored respiration, the pulse becomes slow and soft until imperceptible; with nausea and vomiting, and muscular debility, the symptoms of collapse supervening. Convulsions may occur, the pupils dilate and death ensues from asphyxia. The pulse may become irregular and rapid before death.

Locally, aconitine causes tingling of the tongue, throat, or any part to which it is applied. This is the diagnostic evidence of its presence.

Aconitine has a powerful sedative effect in cases of exaggerated cardiovascular activity, or of irritative cardiac spasm, often observed in the eruptive fevers, and in general in all pyrexias with very high temperature. (Laura.)

Cash states that aconitine alters the cardiac rhythm, in certain large doses, the ventricular systole having no corresponding auricular contraction. Ventricular delirium precedes death.

Two other alkaloids have been found in aconite—benzaconine and aconine.

Benzaconine does not cause tingling or numbness; it slows the heart-beat astonishingly, but a ventricular systole often has two or three auricular contractions preceding it. This is the reverse of what obtains from aconitine. Absolute cardiac quiet for a time, shows interference with the cardiac motor impulses. Blood-pressure is reduced, but benzaconine is lethal through asphyxia. It scarcely affects the sensory nerves but depresses the motor, and checks muscular contraction. The temperature is not much depressed. Dose, 200 times that of aconitine, or 0.02 Gram.

Aconine causes neither numbness nor salivation. It strengthens the ventricular systole and antagonizes the incoordination of aconitine. In very large doses it depresses respiration and suspends the function of the motor nerves. Dose, 2000 times that of aconitine, or 0.2 Gram.

Toxicology.—The beginning of aconitine poisoning is denoted by the sensation of coolness at first, then horripilations in the back, heaviness of the limbs, tension and numbness of the face.

Taking fractional doses of the alkaloid, continued at intervals, we experience successively the following symptoms; numbness and tingling of the tongue, extending to the lips, less to the cheeks, the root of the nose, the forehead; oppression in the temples, light frontal headache; tingling in the hands, forearms and thighs, especially on the outer side; coolness and bristling in the back; the face is red; a sense of excitement like light alcoholic inebriety; appetite normal, often even more than usual.

Diuresis is a little increased, as well as the intestinal peristalsis, without influencing the stools. The brain is unaffected, and the patient can work without difficulty.

The night following the day of experimentation is calm, sleep excellent, and on awaking all traces of aconitism have disappeared.

The pulse oscillates between 84 and 70, the temperature between 99.7° and 98.6° F.

Sphygmographic tracings give no result of value, the drug being taken within physiologic limits.

Van Renterghem found the minimum dose to produce a decided effect to be 1-4 to 1-2 milligram of crystallized aconitine, or 10 to 15 milligrams of the amorphous; while the total dose for twelve hours was 3 1-2 milligrams of the crystallized and 60 milligrams of the amorphous. The strength of each form differs as presented by various manufacturers.

The effects of a lethal dose are thus described by Hookma Tresling: "A colleague had taken 3.6 milligrams of crystallized aconitine, substituted by the druggist for Friedlander's, a very weak preparation. The dose was taken at 4:30 p. m., just after a meal. At 5:30 the doctor found himself ill. He was pale, could hold himself erect with difficulty, mind clear; 8 p. m., pulse small, very irregular, normal rate; skin cool, pupils contracted. He complained of painful muscular contractions, especially of the mouth, burning of the tongue and oppression in the abdomen, precordial anxiety, difficult deglutition, loss of taste, swelling of the tongue, great difficulty in moving or sustaining himself. Intense headache. Sensorium perfectly clear.

"Camphor, coffee and cognac were administered, also digitalis, with mustard to the extremities.

" 'Good God! How cold I am,' said he, repeatedly. In effect, the skin was like ice, especially the extremities.

"He cried, 'I can see no longer!' At that moment his pupils were dilated; they contracted, and his sight returned. The permanent disquiet was characteristic. He then vomited, first spitting up much mucus from the throat. Constantly he complained of the head and the epigastrium. At 8:40 he had the first convulsions, beginning with redness of the face and conjunctivæ, bright eye, then foam on the lips, then involuntary movements of the legs and face, breath stertorous and painful. The paroxysm was short. When over, he asked what had happened and spoke of buzzing in his ears, deafness, and heaviness of the head.

"Ether was then injected. He rolled up his own sleeve. The injection gave him pain. Immediately he cried again, 'How cold I am, I see nothing, colleague.' Pupils much dilated, repeated vomiting; second access of convulsions, more severe and prolonged than the first. He regained consciousness but was exhausted. Seeing the girl who aided us weep, he said, 'Don't cry, I'll be better soon.'

"With difficulty I made him swallow some coffee and cognac. The pulse seemed less feeble. He said his head was on fire and he could not see. He uncovered his arm for an ether injection, and was solicitous about causing trouble.

"At 8:53 p. m., enormous vomiting occurred, cold sweat, the third series of convulsions closed the scene. After this he did not recover consciousness; the pupils were dilated, insensible to light; respiration was shallow and labored. Galvanism was applied without benefit. Respiration weakened, the pulse became imperceptible, the heart stopped, and he died at 9 p. m., four and one-half hours after taking the fatal dose."

There is no evidence that the stomach was washed out or atropine or strychnine administered.

In other cases the following additional symptoms were noted: Dicrotic pulse, eructations of gas, mental confusion, frontal and facial pains augmented by the least exercise of the brain, dyspnea, pollutions, vertigo, rarely somnolence.

From the foregoing description it will be readily understood that the picture of aconitine poisoning is a complicated one; if a sufficient dose has been taken the entire central and peripheral nervous system will be affected and in no well-defined manner. Thus one case will present one set of urgent symptoms and the next another. As it is not impossible for the practician to get a case of accidental poisoning from the chewing or swallowing in some manner of the root or other portions of the larkspur or monkshood plants, which are fairly common in gardens, he should remember that the most likely symptoms will be nausea, retching, with excessive salivation, burning of the mouth and fauces, and diarrhea. Next may appear muscular weakness, slow, weak pulse, and the tingling and burning pass away as the stage of anesthesia begins. At this period there is apt to be great restlessness. Incoordination, vertigo, lividity and coldness of the surface mark this stage—which is usually the second one though if any large amount of the poison has been taken it may be the first apparent. The ingestion of a still larger quantity usually means almost "sudden death," from failure of the heart-action, that organ being speedily paralyzed. In the ordinary case, however, death is more apt to come from respiratory than cardiac failure, and convulsions in this condition are not uncommon. Speech and the special senses may be affected, though intelligence usually remains unimpaired to the end. The drug has been used of late for suicidal purposes, but the symptoms are so unmistakable as a rule that it is not a favorite with criminals. The

symptoms of aconitine poisoning may appear within five minutes and are seldom delayed more than half an hour. Heat is essential in the treatment, and the heart and respiration must be supported by heroic measures during the attempts at elimination, which should always be made.

The general antidotes to alkaloids are iodine, alkalies, tannin (pure), or coffee, or tea, which contains tannin. In a case of overdose of aconitine Burggraeve gave six granules of caffeine and a cup of black coffee, and in one hour the toxic symptoms had disappeared. Free diuresis followed. He asserted that it was much easier to treat poisoning from an alkaloid than from a tincture or an extract, whose effects were less certain as to quality and hence not so readily counteracted. Gubler advises strychnine and the convulsants as antidotes to aconitine, but Burggraeve thought these might be themselves perilous in the state of prostration in which the patient would be found.

Caffeine offers no dangers of its own, and is specially applicable as it relieves the formication and the headache. This is why it is so useful in migraines, with turgescence or cerebral hyperemia. However, we must remember that in grave cases atropine exactly antagonizes the lethal powers of aconitine, and may save life that would be lost under less powerful antidotal medication; for aconitine primarily excites cardiac inhibition, and atropine sedates it. Aconitine induces cerebral anemia, atropine sends a plentiful supply of blood into the cerebral capillaries and holds it there.

Therapeutics.—The chief therapeutic indication for aconitine is the presence of hyperemia, or active congestion, the first stage of inflammation. The reason for the use of this agent lies in its power of reducing the heart-action, lessening the quantity of blood thrown into the arteries, and of relaxing the vasomotor spasm in the skin and elsewhere, allowing the blood to flow back into these channels and thus reducing the over-supply in the hyperemic area. It is therefore in the first stage of all inflammatory attacks that aconitine is to be administered, in small doses rapidly pushed, until the full physiologic effects are manifested. The earlier the remedy is given, the more effective it will be. Pleurisy, pneumonia, bronchitis, peritonitis and local inflammations everywhere, demand this treatment.

When consolidation has occurred in pneumonia, aconitine cannot be expected to dissipate the disease and cause the return of effused materials to the blood; but along the margin of the hepatized tract there is a zone of hyperemia, by which the affection gradually

extends into the surrounding tissue. This is favorably influenced by aconitine, hence we find it useful through the stage of hepatization, as well as in moderating the heart-action when excessive and relieving the engorgement of blood in the unaffected portions of the lungs.

In specific fevers aconitine is most useful as a palliative, keeping the heart-action and fever from becoming excessive, moderating the symptoms though it may not affect the microbic causes.

The dose of aconitine (Abbott), the best for use, is one to three milligrams, for an adult, repeated every ten to sixty minutes till the effect is evident, then as necessary to sustain it. It is always best to give aconitine in solution, to insure quick absorption. To children it may be given by Shaller's rule: One granule, gr. 1-134, for each year of the child's age, and one extra "for the glass," in twenty-four teaspoonfuls of water; the dose of this solution being one teaspoonful every ten to sixty minutes. For children under one year, the best plan is to divide the dose by the weight. A child at one year averaging 15 pounds, the dose for a year may be divided by the child's weight, so that a child weighing seven and one-half pounds receives one-half the yearling's dose, regardless of the age.

In the vast field of febrile disease aconitine holds the first place as an antipyretic. As soon as the bowels have been emptied and disinfected, aconitine should be administered in doses of one milligram (0.001) every ten to sixty minutes, until the fall of temperature, the slowing of the pulse and other indications show that the full physiologic effect has been secured, after which the doses are repeated often enough to keep up the desired effect. The relaxation of arterial tension affords relief to the heart, removing one of the principal obstacles it has to overcome. Digitalin is frequently added to steady the heart, veratrine to stimulate the eliminant apparatus, and strychnine arsenate to increase vitality.

A very important application of aconitine was suggested by Burggraeve—as a preventive of inflammatory accidents following severe surgical operations and accouchements. Thanks to this medicament the patient after the ordeal is calm, and fever does not arise. Many examples of the successful application of this principle appear in the writings of the European dosimetrists.

When there is neither fever, phlegmasia nor acute crisis, but it is desired to act mildly upon the great organic systems and the blood, too poor in vital elements to permit proper function and support the organs, give aconitine at long intervals, two or three hours

apart, one granule at each dose. In hyperesthetic insomnias give on going to bed two or three granules with two of hyoscine and one or more of digitalin, to obtain a sound and peaceful sleep.

In sudden congestions from exposure to cold and wet, with consequent chills, headache, stoppage of menstruation, etc., the prompt use of aconitine will generally restore the circulatory equilibrium and bring back the flow, averting a serious illness.

In neuralgic maladies we have usually vasomotor spasm of the cutaneous capillaries, the skin pale, cool and shrunken, the pulse small and tense. Here also aconitine exerts a most prompt and favorable action, restoring the blood to the skin and relieving congested nerve centers.*

In gastrointestinal maladies aconitine is of great value, subduing the local congestion and promoting resolution. In fact, to enumerate all the maladies in which aconitine is useful would be to list nearly all the diseases to which humanity is heir.

In all cases, it is necessary that the physician comprehend exactly the effect he desires, and that the doses be given in frequency proportioned to the acuteness of the attack and the need for haste, until the desired effect is manifest. In general, a temperature fall to or below 102° F. should be secured and a pulse not over 90, before the remedy is to be given less frequently; but if the fever is evidently subdued, the patient sweating, pain relieved, pulse soft, the time for less frequent dosage has arrived. Few nurses fail to comprehend this simple direction: Give the medicine less frequently after the fever breaks; just enough to keep it down.

Aconitine has been used by many thousands of American physicians in the past fifteen years. One house has in that time sent out more than 50,000,000 granules of this alkaloid, and not a solitary case of fatality or of alarming toxic symptoms has been reported from its use. On the other hand the activity of these granules may be readily tested by allowing one to dissolve in the mouth, when the numbness appears promptly. In view of this statement, the superstitious dread with which this alkaloid has been regarded by many, may be safely laid aside.

Van Renterghem, speaking of synergists and antagonists, says: "In its excito-motor action aconitine acts in harmony with strychnine, brucine, caffeine and quinine; while in other respects it finds synergists in veratrine, colchicine and delphinine. It has no true antagonists." The secondary action of aconitine upon the cardiac

*Alexander (Munch. Med. Woch, 1909, No. 50) says that in facial neuralgias aconitine is indicated, and will prove of value after the usual remedies fail. He insists on the importance of energetic elimination.

functions may be opposed by curarine, and by atropine; which, paralyzing the inhibitory fibers of the pneumogastric, suppress the action of aconitine. These two agents are but partially antagonists (Laborde and Duquesnel).

Van Renterghem says that aconitine, by its sedative action on the vasomotor centers, slowing the pulse and the heart-beat, occupies the first rank among defervescents; while its power of reducing the caliber of dilated capillaries makes it the antiphlogistic *par excellence*. By its use losses of blood can be stopped, while its anesthetic power over the nerves of sense gives it an honorable place as an antineuralgic. With strychnine and digitalin, Burggraeve pronounced it invaluable as a preventive of fever and inflammation, in puerperal and surgical cases. He gave it in the evening, to prevent or moderate the physiologic evening rise and insure rest. This he termed "equilibrating the physiologic balance." Van Renterghem finds aconitine of value in breaking up incipient catarrhs and quinsies. With digitalin it is a powerful diuretic. With veratrine it combats fevers in the sthenic forms; it is combined with quinine in malaria, with digitalin for irregular hearts in acute maladies, with caffeine in somnolence and torpor, with strychnine to prevent depression and arouse vitality. It calms agitation, delirium, insomnia and nervousness. In alcoholic delirium it acts like magic when combined with digitalis, strychnine, hyoscyamine or morphine. In the deliriums met among the insane it is of like benefit. As an antineuralgic aconitine has marvelous success with hyperemic forms; not only in trigeminals but in neuropathies of central origin. It relieves toothache, even by inserting a granule in a carious cavity, alone or with one of hyoscyamine. In diathetic neuralgias the appropriate remedy must be given with the aconitine, such as quinine, arsenic, iodine, salicylates, etc. In chronic cases, catarrhal asthma, rheumatism, arthritic pains, old neuralgias, congestive amaurosis, associate it with iron, arsenic or zinc. It is efficacious in epilepsy and chorea (Burggraeve). Visceral hyperemias call equally for aconitine (Laura). It cures tinnitus aurium.

Laura obtained marked success from aconitine in the treatment of the irritative erethism of the insane, where also with the addition of hyoscyamine the persistent and rebellious insomnia was conquered. He found similar advantages in its use for acute and subacute cerebral hyperemias and solace even in the chronic forms. Good effects followed its use in acute and subacute dropsies, especially when fever was present; aconitine with digitalin and scillitin inducing abundant diuresis.

Brunton enumerates among maladies in which aconitine is useful, pleurisy, pneumonia, phthisis, peritonitis, pericarditis, rheumatic fever, gout, erysipelas, otitis, gonorrhea and urethral fever; also the neuralgia accompanying herpes zoster, amenorrhea from a sudden check of the flow, and severe menorrhagia.

Butler says aconite seems to exert a peculiarly beneficial influence on acute mucous inflammations, with fever, small wiry pulse and rapid heart-action. He finds it most efficient in irritative fevers of children. Thrown into the rectum, it causes slight prolapse and quickly affects an irritable urethral stricture, facilitating catheterism. It has been recommended in cerebrospinal fever; and in aneurism as a sedative.

Murrell pronounces aconite invaluable in the initial stage of all acute fevers. In the eruptive fevers it brings out the rash and mitigates the subsequent severity.

Shoemaker states that aconitine ointment will often assuage the pain of chronic rheumatism, gout and myalgia, cutaneous neuralgias, paresthesiæ, pruritus, papular eczema and prurigo. Jonathan Hutchinson found it mitigated the pains of carcinoma, and also employed it in rheumatic iritis, acute congestion of the brain and spasmodic croup. It is said to antidote the sting of the scorpion. It relieves the pain of epididymitis and gives much relief in tobacco-heart.

Ringer says that spinal irritation, intercostal neuralgia and sciatica yield to aconitine ointment, but more readily to belladonna (excepting sciatica). Its power to control inflammation and subdue fever is remarkable. Aconite at once arrests post-vaccinal inflammation; it checks epistaxis, subdues fluttering of the heart, quiets "fidgets," and is said to remove chordee.

Wood considers aconite the best remedy for cardiac hypertrophy, simple and compensative.

Ellingwood recommends aconite in acute nephritis and cystitis, in the inflammatory stage of dysentery and cholera infantum, in the onset of diphtheria and croup, and in acute mastitis. It heightens the effects of cimicifuga, belladonna, veratrum, gelsemium and asclepias.

Scudder applies the tincture over the eyebrows in acute conjunctivitis with photophobia; and uses it locally also in earache. It is better to use aconitine granules dissolved in water, as the effect of alcohol on the eardrum is injurious.

"Aconitine is a heroic remedy in continued fevers, when administered with the cares already mentioned. Fever is always a

fact that demands the attention of the physician. It is always a danger, a disastrous fire.

"Aconitine may be employed alone or associated with veratrine, quinine, strychnine, as may be indicated. With veratrine it is indicated in all cases of excessive fever, with sthenic and phlogistic symptoms predominating, in young robust subjects, and in obstinate pyrexias. Quinine is indispensable in remittents, strychnine whenever the patient is depressed and the cerebrospinal and cardiopulmonary tone below par, threatening collapse—in which case phosphoric acid and caffeine should be added.

"Employed properly aconitine is an efficacious antipyretic in the most rebellious cases of typhoid fever, even rendering the baths less urgent or unnecessary; it lessens, directs and regulates, finally conquering, the febrile movement.

"In eruptive fevers, with high temperature, the excessive heat (always a menace to life) causes grave structural lesions in the nerve and cardiopulmonary centers and serious blood and renal changes. Aconitine combats these and also opposes the exanthem by its antipyretic power, its diaphoretic action lessening the excessive tension of the cutaneous vessels, lowering temperature promptly, and regulating the vasomotor nerves; thus favoring crisis, the eruption occurring sooner and over a greater surface, and the evolution of the malady being accelerated. But there is no reason for excluding the simultaneous employment of other remedies, when indicated. Such association is not only logical and scientific, but daily experience with it displays excellent results.

"The success of aconitine in the eruptives is the more remarkable since everybody knows that an incomplete or tardy eruption endangers the patient's life by threatening visceral complications, without mention of the irreparable consequences. When treatment has been neglected and the cure is incomplete, health will long be absent, and the patients, dyscrasic, rachitic, marasmic, lead a deplorable existence and suffer ills without end.*

"Aconitine is also very useful in active hyperemias, irritations, congestions, those marking the debut of acute maladies and the secondary hyperemias that accompany dangerous visceral inflammations. It is equally indicated in true and essential plethoras, with or without local inflammations, and here success is won by perseverance in the use of this powerful modifier of nerve-function and of sanguine crasis.

"One of the most formal indications for aconitine is the inflam-

*H. T. Webster (*Medical Council*, 1910, p. 117), found Aconitine locally of value in pruritus vulvae.

matory process, especially in its initial stage, vital and dynamic, before the circulation in the affected part has been impaired and structural changes have occurred irreparably. This indication is found in the mucous affections of the vast respiratory tract, in pneumonia, in the neuropathies of the respiratory organs and in irritations and inflammations of the endocardium. It has a potent sedative effect in exaggerated cardiovascular action or irritative cardiac spasm, frequently manifested in eruptive fevers and all pyrexias with very high temperatures. The same holds as to irritations and inflammations of the nerve-centers, with exaggerated irritability; in headaches, disquiet and agitation, insomnia, delirium, by which the state of the encephalon is shown. It may even be utilized in the most acute crisis of mental disorders.

"As a diuretic and diaphoretic aconitine is serviceable in all affections when the urinary and cutaneous secretions are suspended —not without great danger to the patient—conditions frequently met with in practice. It is useful also in rheumatismal maladies and in the paroxysms of pyretic and tonic gout.

"Aconitine has an important place in the treatment of nervous affections. These, especially when hereditary or engrafted on a dyscrasia, give no respite and often resist treatment; we may then confidently have recourse to aconitine. Very quickly it relieves hyperemic neuralgias, mainly those due to general congestion, or local, of the encephalon, the spinal cord, or some dependent on these two, and it combats the element of pain when this augments the congestion of the affected nerve and the region supplied by it. It can also be used in all neuropathies of centric origin and having their source in a spasmodic ischemia of a vascular nervous tract, direct or reflex; but here we add atropine, to relax the spasm more speedily and to relieve the anemia depending on this vascular spasm; which also causes the most acute sufferings and manifests itself in the motor-sphere by contractures, spasms, or convulsions, local or diffuse. These give way to hyoscyamine, the king of antispasmodics. Similar service is rendered in hyperemic neuralgias, of centric origin, in which intestinal derivatives should be added.

"Aconitine as a dynamic and vital modifier is useful in neuroses accompanied by general debility with anemia, here adding the arsenates of quinine, strychnine and iron, and the general tonics that may be desirable. In neuropathies symptomatic of dyscrasias there should be joined to the aconitine the whole series of hygienic and therapeutic means indicated for each diathesis—iron in anemia and chlorosis, arsenic in paludal dyscrasias,

mercury in syphilis, sodium in scrofula and exaggerated lymphatism, and so forth.

"The arthropathies also demand aconitine, aided by frictions with this alkaloid in petrolatum, covering the part with cotton. If the neuralgic pain is piercing, cicutine may be added with advantage; and in these cases, frequently met clinically, this is a precious dynamic modifier. In intermittent neuralgias with marked exacerbations we add quinine hydroferrocyanide; and for anemia or the paludal cachexia, quinine arsenate. Much of our success will depend upon a good hygienic regimen and the reconstituent alimentation—insisting on pure air, especially rural, moral consolation and repose of mind.

"Aconitine has good and prompt success also in the cerebrospinal hyperesthesias, especially of children, where cerebral exaltation mounts to delirium under the influence of fever. In insomnias caused by cerebral hyperesthesia aconitine secures a sleep calm and recuperative, the patient awaking rested and hopeful of cure—and no physician will deny the benefits of hope."

Laura employs aconitine, with quick results, in gastralgias and enteralgias, especially if rheumatismal. It calms spasmodic phenomena, direct or reflex, dependent on irritation or congestion of any part whatsoever, or on local hyperemias of the nerve-centers. Burggraeve utilized it in clonic convulsions. Van Renterghem advised this remedy in delirium and infantile convulsions, the symptoms due to local hyperemia of the nerve-centers. Burggraeve also recommended it in chronic cases—asthenic catarrhs, chronic rheumatism, arthritic pains, chronic neuralgias, congestive amenorrhea, alone or with other indicated remedies. Laborde succeeded with aconitine in acute articular rheumatism and in protopathic facial neuralgias.

One symptom most tenacious and disagreeable is roaring in the ears, often without appreciable pathologic condition of the auditory apparatus or of the nerve-centers; no known cause being assignable, it is placed among the neuroses. But this is completely cured by the persistent use of aconitine, when there is no contraindication and no recognizable material cause that is incurable and persistent.

In numerous cerebral arterial hyperemias, acute or subacute, we may give aconitine with advantage; and it is even useful in the chronic fevers. It has given good results in acute and subacute dropsies, especially with fever, through the free diuresis induced; digitalin and scillitin being added.

Professor Laura insists upon the accurate fitting of the dose to the needs. He protests against the idea of maximum and mini-

mum doses. Our rule is to fit the quality of the medicine to the *nature* of the disease, the quantity of the medicament to the *entity* of the malady or its resistance. In brief, we give "*dose enough.*"

When fever runs very high and the vital organs are in peril we give one or many granules, repeating every fifteen minutes; lessening the number of granules and increasing the intervals as the force of the attack gives way, as calm is reestablished, the cardio-vascular system sedated, the skin becomes softer and moist, the temperature falls to about 100° to 102° F., the urine freer and the suffering evidently diminished. In febrile and inflammatory maladies when the fever is not above 102.2° F., one granule at each dose will suffice. The same suggestions serve in neuropathies, cerebral hyperesthesias, etc.

To adults aconitine may be given in water, soup or diluted wine. Do not break up the granule in the mouth or else a disagreeable sensation will result. For infants under two years dissolve the granules in milk, one in two teaspoonfuls, and give as desired.

Never, under any circumstance, administer aconitine hypodermatically!

Stop the use of aconitine in acute fevers when you have obtained a durable defervescence; in painful maladies when there is sedation; in chronic cases when the pulse falls to the normal point, with the sensation of cold; when you note enfeebling, even slight, of the cardiac rhythm, dilation of the pupils, diaphoresis, diuresis; when, in one word, the lowering of vital energy is a symptom more or less evident of hyposthenia.

Aconitine is eliminated in part by the bowel, and to avoid cumulation the use of a daily saline laxative is advisable.

In the above presentation we have closely followed Prof. Laura, giving literally the views and usually the language of the great Italian clinician. In the main his conclusions are those of other observers, including ourselves. Laura seems, however, to have been dominated largely by the dread of aconitine as a dangerous poison, expressed by the older therapeutists and still felt by those who have not rendered themselves familiar with this alkaloid.

However, danger lies only in rashness, ignorance and uncertainty; it can never pertain to the intelligent use of any remedy of certain and unvarying nature. If we give exactly enough tincture of aconite to do the work, and then have our prescription refilled with a tincture much stronger, we shall assuredly be convinced that aconite is a dangerous remedy. This can never be the case with aconitine in standard granules.

ADONIDIN

Standard granule—Adonidin, gr. 1-67, Gm. .001.

Adonidin is described by Merck as a glucoside from the root of adonis vernalis. It is a light brown, very hygroscopic, readily conglutinating, odorless powder, intensely bitter. Soluble in water, alcohol, fusel oil; insoluble in ether, chloroform. It is a cardiac stimulant and a mild diuretic. Merck gives its indications as heart diseases, in place of digitalis; nicotine intoxication, chronic diffuse nephritis. It is said to be especially useful in mitral and aortic regurgitation and for the relief of precordial pain and of dyspnea.

Adonidin is described by Van Renterghem as a glucoside, colorless and odorless, very bitter, rapidly dissolving in alcohol, slightly soluble in water or ether. Cervello ranked it with digitoxin. As this is a powerful toxin Van Renterghem made experiments on himself, employing Merck's adonidin. He found physical properties differing from those reported by Cervello, Merck's product being a yellowish brown powder, with a spicy odor.

On the first day he took 1-2 milligram every two hours for six doses; on the second 2 milligrams every two hours for five doses; on the third the total dose taken reached 40 milligrams, three every hour; on the fourth he took a centigram four times; on the fifth 6 centigrams in twelve doses. During this period he had no subjective symptoms, all the bodily functions progressing as usual. A notable slowing of the pulse occurred on the fourth and fifth days, from 70–80 to 58 and 62, on the fifth evening. On the morning of the fifth and sixth days it returned to normal. Sphygmographic tracings showed under the influence of adonidin a diminution of the amplitude of the pulsative projection, the formation of a horizontal plateau and a uniform descending line, as with digitalin. He concludes that the adonidin of Merck is a body of much less energy than that with which Cervello experimented; that it presents the physiologic action of pure digitalin, giving no cumulative phenomena, and might advantageously replace the active principle of digitalis. He proposes as a tentative dosage two to three milligrams—gr. 1-30 to 1-20—repeated every quarter hour, of Merck's adonidin.

It must be said here that it is unwise to trust too implicitly to the claims of a lack of cumulative tendency in the succedanea of digitalis. The very few trials made of these rarely employed and little-known agents might not happen to show cumulation; but if they were employed as frequently as digitalis, the cases in which this accident occurs would be found.

The National Dispensatory says that the adonidin of the shops is a mixture of five principles, of which picradonidin, a glucoside, is the active one, a powerful heart poison. Adonis is chiefly used as a succedaneum to digitalis; it is irritating to the mucosa and may cause vomiting and diarrhea; it slows the heart, increasing the force of its beat, raising vascular pressure; and acts as a diuretic, increasing mainly the water of the urine. It has been given with asserted success for cardiac dropsies when digitalis had failed. The dose advised is gr. 1-10 to 1-4 of adonidin.

Felter and Lloyd say that adonis stimulates the heart muscle, increasing cardiac contractility, and by contracting the smaller arteries universally it increases arterial tension. It slows and regulates the heart-beat. It acts more quickly than digitalis and is well tolerated. The diuresis is due to the effect on the renal arteries. Large doses paralyze the heart and blood-vessels. It is not cumulative. Gastrointestinal inflammation is a contraindication. It is adapted to cases where the heart muscle is laboring to overcome a valvular obstruction, and when dilatation is threatened. Hale found it also useful in the cardiac complications of nephritis, with weak irregular pulse, intermittent, venous stasis and dropsy. In chronic albuminuria with scanty light-colored urine and delirium it was of benefit; also in a case with uremic convulsions it gave satisfactory control. Scudder advised adonis in heart strain from overexertion. Benefit was evident within one day after beginning its use. Pallas pronounced it an efficient emmenagog.

Specific Indications.—As a heart tonic, when cardiac action is weak, with but little blood in the arteries, low pressure and short diastole, venous fulness and stasis with increased pressure; feeble, intermittent, irregular pulse; valvular insufficiency with regurgitation and dropsy; vascular enfeeblement with passive, dull, congestive headache; chronic congestion.

Durand recommended adonis in mitral insufficiency, interstitial myocarditis and palpitation. Ellingwood found it induced diuresis when digitalis had failed, and proved of value in dyspnea from feeble heart. Bekhtereff praised it as a remedy in epilepsy, and this may be true if the circulation needs toning. Codeine and potassium bromide were given simultaneously.

Shoemaker calls attention to the decided fall of arterial pressure induced by overdoses, with paralysis of the heart and vessels. Da Costa spoke well of its action on functional irregularity of the heart, and in cardiac asthma. Shoemaker says that adonidin acts less powerfully than digitalis, but Bartholow declares the former is

the more powerful. Both say it acts more promptly. The diversity is probably due to the quality of the specimens employed. Durand reports a case where three grains were taken every half-hour, the result being active gastrointestinal irritation. Oliver found that it gave relief to precordial pain, as well as to dyspnea and palpitation in mitral and aortic insufficiency.

Dr. Heinrich Stern (*Medical Review of Reviews*, 1910, page 76) who recommends the addition of a cardiac tonic to thyroid whenever this preparation is to be used for any length of time, expresses a decided preference for adonidin; recommending the following formula:

Sodium cacodylate.....	1-200 grain
Adonidin.....	1-30 grain
Thyroid gland (dry powder).....	1 grain

For one compressed capsule.

If fresh adonidin cannot be obtained, caffeine may be substituted in doses of 1-6 of a grain.

ÆSCULIN

Standard granule—gr. 1-67, Gm. .001.

From the horse chestnut, Æsculus hippocastanum, is derived Æsculin, a bitter glucoside. The bark yields about 2 to 3 percent. In the galenic preparations æsculin is associated with several other active principles, such as saponin, which, existing in variable amounts and proportions, render their action too uncertain for modern medicine. The glucoside has not been extensively employed but from the meager reports upon it we gather what follows:

Therapeutics.—Æsculin is a bitter tonic and has the virtues of the plant. By the eclectics it is valued in malarial fevers and especially in visceral neuralgias, when abdominal plethora coexists. It is not a remedy for acute conditions but for chronic capillary stasis, general vascular fulness, soreness and throbbing with malaise; uneasy, full, aching sensation in the liver, rectal irritation and hemorrhoids, with constriction and congestion, spasmodic closure of the sphincter, itching, heat, pain or simply uneasiness. The piles are large, purple, do not bleed, but there may be diarrhea. Æsculin relieves these conditions, and also rectal neuralgia and proctitis dependent thereon, as well as such reflexes as dyspnea, asthma, vertigo, headache, backache, etc. (King.) As æsculin relieves the rectal affection these difficulties subside.

Scudder says that æsculus glabra is sedative to the pneumogastric and respiratory nerves, acting probably most upon the

spinal system. It is indicated by sensations of tightness in the chest, and about the precordia; asthma with continuous difficulty in breathing; tightness and constriction in the rectum with uneasiness; hemorrhoids. This form of asthma is not paroxysmal; the difficulty of breathing being persistent though worse at times. He also recommends it in phthisis with difficult breathing and oppression. When the special indications for this remedy are present with hemorrhoids it proves very useful—these are a peculiar irritation in the small intestine, with contraction and colicky pains about the umbilicus, with intestinal dyspepsia persisting for weeks. Small doses suffice for the cure.

The writer's attention was especially directed to æsculin by a traveler for a drug firm, who remarked that "whenever he could get a doctor to try æsculin he was sure of a customer." The symptoms described by Scudder are usually associated with a chronically enlarged liver, painless, not alcoholic but apparently due to a sedentary life with a special liking for meats. In this condition, with sluggish hemorrhoids, easily aroused to irritation by minute doses of aloin or of cascara, the use of æsculin has not yet failed to bring relief. The doses used have been small—gr. 1-67 seven times a day, with three more granules at bedtime, making ten, or a centigram, each twenty-four hours. This is continued for one month. The results have been such as to confirm the recommendation.

Æsculin is soluble in 672 parts of cold water, 12.5 of boiling water and in 24 parts of alcohol. The dose for periodic fevers is 5 to 30 grains, but for hepatic obstructions it is recommended in very much smaller doses.

AGARICIN

Standard granules—gr. 1-67, Gm. .001; gr. 1-12, Gm. .005.

Agaricin or agaricic acid, C_{14} H_{27} (OH) $(COOH)_2$, is derived from the Boletus laricis, or larch fungus, known also as Polyporus officinalis. The fungus, which is of horse-shoe shape, is gathered in August and September. Agaricin is obtained in silvery, lustrous crystals, tasteless, soluble in ten parts of hot, in 130 parts of cold alcohol; insoluble in cold and slightly soluble in hot water, in ether or chloroform. Jahns obtained agaricic acid by submitting white agaric to the action of hot alcohol. The product was 16 to 18 percent, mixed with 4 percent of a crystalline matter, 3 percent of an amorphous white substance, and 30 percent of a purgative resin.

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Fleury reduced the agaric to powder, and treated it with absolute anhydrous ether, obtaining an amorphous resin and agaricin in very fine needle crystals.

Physiologic and Toxic Actions.—Agaricin and its sodium salt irritate the mucosa and may cause suppuration if injected. Large doses cause vomiting and purging, especially if the agaricin is impure, containing resinous matter. In toxic dose injected intravenously, agaricin first stimulates and then paralyzes the medulla, the blood-pressure rising and then falling, the heart first slowed by inhibition, then regaining its rhythm, finally failing after the arrest of respiration (Cushny). The arrest of perspiration is due to action on the peripheral nerve-ends, as with atropine, but agaricin acts only on the sweat-glands and has none of the disagreeable effects of atropine on the pupil, mouth and skin. It is used only as a remedy for sweating, especially the night-sweats of consumption. It is less effective in miliary tuberculosis (Liebreich). It has no effect on the pulse, temperature or respiration. In non-tubercular affections agaricin is almost always effective in checking profuse perspiration. Pure agaricic acid is soluble in oil of turpentine, and might be thus given with advantage in typhoid fever. It should be given in a single dose, five hours before the time for the expected perspiration. The patient soon becomes accustomed to agaricin and the dose must be increased. No bad effects have been recorded from its continued use. Atropine antagonizes agaricin, gram 0.01 (gr. 1-6) of agaricin fairly counteracting gram 0.0005 (gr. 1-134) of atropine (Proebsting).

Therapeutics.—Merrell recommends agaric in obstinate remittents, with brief chills and prolonged fever, little or no sweating, but jaundice, aching back and joints. Small doses should be given.

Kopp found it especially valuable in restraining the copious sweating of arthritics; and Grant claimed for agaric antirheumatic properties. The older writers seemed at sea as to the cathartic effect of agaric, numerous contradictory statements appearing in their pages. Gubler even contradicts himself; for while he attributes its anhidrotic effect to derivation by purgation, he says that this fungus has been wrongly ranked with the drastics, since doses of four grams may be given without producing apparent purgative effects.

This is easily explained, as the purgative principle is the resin, while the anhidrotic power lies in agaricic acid.

Seyffert pronounced agaricin as efficacious as atropine against hectic sweats, and much less toxic.

Proebsting denied that four hours were necessary to develop the full effect of agaricin, which he found to act very promptly.

Van Renterghem advises that agaricin be alternated with atropine or picrotoxin, to avoid the necessity of using large doses. Or, these agents may be given in combination.

Hofmeister gives the dose of pure agaricin as 0.004—0.02 (gr. 1-16—1-3).

Merck recommends agaricin in doses of 0.015—0.065 (gr. 1-4—1), and pure agaricic acid preferably, 0.01—0.032 (gr. 1-6—1-2). He speaks favorably of its use for sweating from overdoses of the coaltar antipyretics.

Briefly, agaricin is anhidrotic, antiperiodic, a stimulant to the nervous system, and in large doses cathartic and emetic—the latter effects should never be produced with this drug. In some obscure aches of the back and limbs agaricin will give prompt relief.

Hofmeister advocated it as a singularly differentiated remedy, acting solely on the sweat glands. The alkaline combinations are freely soluble.

Seyffert found hypodermatic injections of agaricin too painful to be endured, and the time required for action not shortened.

Shoemaker says agaricin has been used to suppress the secretion of milk. It acts on the abnormal sweating of phthisis and that from other causes. Anders combined it with quinine and antipyrin. Hofmeister found that in warm-blooded animals it caused somnolence, prostration and slow respiration.

The wide variance between the reports as to the efficacy of agaricin as a remedy for abnormal sweating may be due to differences in the quality of the specimens employed, or to the different doses given. Too large doses may defeat the object by inducing vasomotor paralysis, neutralizing the action on the sudoriparous glands.

Combemale makes the following statements concerning this substance:

1. Agaricin is antisudoral, acting promptly against all kinds of exaggerated sweating, so, too, against the sweating of the tuberculous, especially in the second and third periods.

2. The use of agaricin is not accompanied by any inconveniences in the digestive tube of a kind that were not present before the administration of this drug.

3. The anhidrotic action of agaricin begins two hours after its administration, reaches its maximum two hours later, and ceases at the end of eight hours.

4. It is not necessary to increase the dose of agaricin in order to obtain its full antisudoral effect, which shows that it has no habituating action.

5. Neither has agaricin cumulative action, which makes possible its administration for as long a time as it may be indicated.

How does agaricin act? According to Hofmeister, by paralyzing the peripheral nervous apparatus of the sudorific glands. Its action is produced with small doses, not enough to affect the central nervous system at all nor the grand sympathetic. It does not moderate either the salivary or lachrymal secretions. It does not modify either the rhythm or the frequency of respiratory action. Lastly, it does not seem to influence the functions of the skin nor the exhalations from the lungs. The last result is explained by the fact that there is less thirst while one is taking agaricin, consequently much less water is ingested.

When does the agaricin produce its effect? At the moment of being absorbed or at that of its elimination? It is very probably at the moment of elimination, since it does not begin to act until two hours after ingestion and lasts during the entire period of its elimination. That which speaks most in favor of this interpretation is the fact that the action of agaricin does not persist beyond eight hours, and inasmuch as it has no cumulative action it is not maintained after that time.

Agaricin is not the only medicament which is prescribed against excessive sweating. Quite a number of more or less value have been lauded for that purpose. Thus the astringents, tannin, rhatany, and acid lemonades, etc., are prescribed. Acetate of lead is not altogether harmless. Martin, of Munich, gives 50 centigrams (gr. 7 1-2) of sulfonal in the evening against phthisical sweating, but the prolonged use of this drug is fraught with great danger. Ergotin is an incontestably efficacious medicament, but when long administered gastrointestinal troubles are sure to appear. The same is true of hydrastis, which also diminishes the pathologic perspiration of the tuberculous but weakens the digestive canal.

For some years acetate of thallium has been extolled, but it has the great objection of inducing falling of the hair and exposing the patient to alopecia.

Atropine is the most powerful antisudorific prescribed, but its activity should warn against its use except with great precaution. Moreover, it not only suppresses the perspiration but all other secretions—saliva, tears, and so on. Its administration is not without inconveniences when it has to be used for any length of time.

It is not so with white agaric, which has enjoyed a great reputation for a long time past. Haen, Andral, Trousseau and Peter employed it frequently. The objection to agaric is that its effect does not last long, and it has to be repeated periodically. It is better to have recourse to agaricin, which is free from this inconvenience (Vigouroux).

ALETRIN

Standard granule—gr. 1-6, Gm. .01.

Aletrin is a concentration from the rhizome of aletris farinosa.

The dose of aletrin may be placed at gr. 1-6 to 1-2 before meals. For dysmenorrhea give gr. 1-6 every fifteen minutes in hot water till relief.

Lloyd says that so universal has the confounding of plants been that King in describing the root of Aletris has given a description of Chamaelirium, while Strong's American Flora figures the top of Aletris with the rhizome of Chamaelirium. Ellingwood, however, says Aletris is conspicuously active in uterine affections, being indicated by extreme weakness in the uterine structures, with general feebleness from overwork, sexual indulgence or too frequent childbearing. In hyperactivity of the womb and ovaries from lack of tone, deficient menstruation or sterility from this cause, pale scanty flow at protracted intervals; anemia and chlorosis with insufficient menses in young girls, aletrin is of great service. Give it for specific effect with iron and other tonics indicated. Under such circumstances its direct influence on the pelvic organs is sometimes magical. It acts promptly on prolapsus or retro- or ante- versions with relaxed and feeble tissues. Its benefits are conspicuous in emaciated and enfeebled women. It improves the functions of the ovaries, overcoming sterility and correcting habitual abortion promptly. It is a reliable remedy for extreme nausea of pregnancy with fainting. Unfortunately aletrin has usually been given with a group of allied remedies, so that whatever special virtues it may possess have been hidden in the clouds of polypharmacy.

ALNUIN

Standard granule—gr. 1-12, Gm. .005.

Alnuin is a concentration from the bark of Alnus serrulata, the tag alder. The bark contains tannic acid, oils and a resin, the latter forming the bulk of alnuin.

King says that this agent powerfully increases retrograde

metamorphosis, and is tonic to the mucosa, aiding digestion and assimilation. It is catalytic and antiputrefactive. It increases the flow of gastric juice. It is alterative, emetic and astringent.

The eclectics recommend alnuin in scrofula, glandular enlargements and suppurations, superficial diseases of the skin and mucosa as in eczema or pustular affections (Scudder), impetigo, herpes, prurigo, scurvy, scurf of the scalp in children, boils, passive hemorrhages, hematuria, purpura hemorrhagica, marasmus, mothers' sore mouth, indigestion and dyspepsia with deficient secretion of gastric juice and gastric motility, diarrheas attending the above gastric condition, leucorrhea, mammary indurations, hay fever (Ayer), gonorrhea and rhus poisoning. Where possible it should be employed locally as well as internally. The specific use is to improve nutrition and increase waste, in scrofula and scaly or pustular chronic skin diseases.

We have found this drug useful for women who are sallow and muddy except when menstruating. The use of alnuin clears up the complexion and renders it of a waxen brilliancy.

The dose is gr. 1-2 four times a day, increased if necessary till effect.

Dr. E. F. Bowers, of New York, gave alnuin with potassium iodide in a case of leg ulcer of twenty-two years' standing, with local antiseptics. A cure was secured in three months.

Dr. B. S. Horne considers alnuin superior to arsenic as a remedy for a bad complexion. In eczemas with feeble vitality he finds its effects surprising. Webster mentions a Thompsonian who relied almost wholly on alnus in all chronic affections and won phenomenal success. He claims for it a special affinity for the skin, influencing its nutrition. The reports point to the remedy as increasing cutaneous elimination of solids.

ALOIN

Standard granules—gr. 1-12, Gm. .005; gr. 1-6, Gm. .01.

Aloin is obtained from the Aloe spicata, Aloe socotrina and Aloe vulgaris (Nat. Ord. Liliaceæ). Hitherto the dried juice of the leaves was the preparation used in medicine. This consists of aloin, aloetin and aloetic resin, all cathartic, with a small proportion of gallic acid, fat and albumin, together with waste matter.

Aloin is obtained by evaporating an aqueous extract in vacuo. It occurs in small colorless crystals of sweetish bitter taste. It forms but a small proportion of aloes. It is inactive in the bowels while crystalline (Schmiedeberg).

Aloetin is an amorphous aloin, and is more active. It forms the bulk of the aloes.

Aloin dissolves freely in formamide, in 60 parts of cold water, 20 of alcohol, in hot water and hot glycerin, in the latter being transformed into aloetin. It belongs to the aromatics, since with caustic potash it splits up into paraoxy—benzoic, acetic and oxalic acids.

Physiologic Action.—In doses of 0.01—0.06 (gr. 1-6—1) aloin increases the gastric secretion and motility (Liebreich).

Nothnagel denies that aloes requires bile to develop its cathartic activity, though he states that aloes and oxgall, or aloin and glycerin (Kohlstock), injected into the rectum, act as a cathartic. Nor does he admit the stomachic and digestive powers credited to aloes. But in these respects Liebreich differs with him.

Von Magyary has shown experimentally that aloin administered hypodermatically and in small doses produces an increased rate in the metabolism. (*Rev. Ther. Monatsh*, 1910, page 385).

In doses of 0.1—0.5 (gr. 1 1-2—7 1-2) aloes causes eructations, gastric oppression, and in about twelve hours several dark, mushy stools, usually with some griping. Three times this dose does not cause catharsis more quickly, but more griping and rectal tenesmus, and the stools are more fluid. Aloes stimulates peristalsis strongly, especially in the lower bowel, and probably increases the excretion of bile, by a similar action on the walls of the gall-ducts. The continued use of aloes does not beget tolerance, but the contrary; so that when given continuously the dose may be gradually reduced, the same effect being manifested.

Aloes induces an afflux of blood to the rectum, uterus and ovaries, inducing or aggravating any existing tendency to hemorrhoids, hemorrhage from the rectum or uterus, abortion or strangury, and it strongly stimulates the sexual appetite and functions. It is therefore contraindicated in hemorrhoids, pregancy, menstruation, erotism, tendency to menorrhagia, dysentery, nephritis, cystitis, and all pelvic engorgements. However, this does not apply to hemorrhoids with atony of the rectal sphincter and prolapse, in which minute doses of aloes are especially useful.

Aloin is actively cathartic in doses of 0.1—0.2 (gr. 1 1-2—3), whether administered by the stomach, the rectum or subcutaneously, though it is milder when given hypodermically. It is then excreted into the bowel, acting locally there (Cushny). In large doses it is violently and painfully cathartic. It enters the blood, as the milk of a nurse taking aloin acts on her nursling's bowels.

Aloin differs as it is derived from the various forms of aloes brought to the market, the Socotrine, Cape, Barbadoes or hepatic; the former being probably the best. It occurs in small, bright, sulphur-yellow, prismatic needles, containing 1-2 an equivalent of water.

Therapeutics.—Aloes possesses the unique property of gradually increasing the tonicity and irritability of the muscular elements of the larger bowel. Given in doses of 0.005—0.06 (gr. 1-12—1) three times a day, or 0.001 (gr. 1-67) every hour until the bowels move, it will be seen that the dose found sufficient to produce a daily action can be gradually diminished, until at length the drug can be altogether discontinued. The powerful influence of habit should be secured, the patient being enjoined to go to the closet at the same hour every day. The tendency to griping may be lessened by adding a minute dose of atropine, while the peristaltic action is enhanced by strychnine, the irritability by capsicum. The following granule has proved very popular:

Aloetin .....gr. 1-67
Strychnine sulphate .....gr. 1-134
Atropine sulphate .....gr. 1-5000
Capsicum oleoresin .....gr. 1-67

M. S. One every hour till the bowels move; or three to six before each meal.

These may be depended upon to cure any case of chronic constipation not dependent upon mechanical obstruction.

Aloes is emphatically a remedy for small doses, frequently administered. There is no legitimate use of this drug that requires a dose larger than one grain.

When hemorrhoids of long standing cease to bleed and symptoms of cerebral hyperemia appear, aloes will give relief by restoring the hemorrhoidal flux.

Aloes is sometimes employed as an emmenagogue in constipated, anemic women of frigid type, with scanty flow. It is also added in minute doses when iron or other constipating drugs are administered.

The griping caused by aloes is much lessened by giving it after meals. Cushny suggests that the bile may aid the action of purgatives by rendering them soluble, or by delaying the solution until they reach the lower bowel.

King says that aloin purges if it is applied to the surface of an ulcer or blister. Kohlstock found the solution in glycerin or in formamide relieved mild constipation when applied to the rectum,

in doses of gr. vj to vijss. But this degree of effect would result from the glycerin alone.

For ascarides the aloetic solution should be injected past the sigmoid flexure into the colon, as these parasites flourish near the ileocecal valve.

In chlorosis, iron should be combined with the aloin; in hysteria add asafetida; in amenorrhea give four days before the time for the menses, with iron and myrrh; for acholic stools add podophyllin or calomel; while for melancholy, hypochondria, and the group of symptoms usually attendant, give with intestinal antiseptics, and see to the condition of the prostatic urethra. For chronic atonic diarrheas give the smallest doses, gr. 1-12 or less, with sulphur and atropine, also in small doses.

When costiveness is the cause of the constipation, aloes can do nothing but harm. It seems to have little or no good effect on flatulence, which is a surprise. But the addition of quassin and charcoal makes an effective combination.

AMMONIUM CHLORIDE

This salt, once known as Dutch calomel, increases the secretions along the alimentary tract, especially the bile; and is depurative, lessening the solid elements of the blood. It acts on the mucosa generally, increasing their secretions and promoting nutritive changes and epithelial exfoliation. It is eliminated by the kidneys, skin, bronchi and other mucosa, feebly stimulating them. It increases all the urinary solids except uric acid, which it slightly lessens.

Butler values this salt very highly in bronchitis after the first stage has passed; also for the aged and feeble. It has seemed useful in whooping-cough but we have better remedies. It has been used for intermittents, and to promote eruption in the exanthemata. In goiters it acts as an absorbent, and has also proved effective in some forms of amenorrhea and dysmenorrhea, especially in plethoric types. In neuralgias it has won an undeserved reputation from its powerful effect in myalgias, of the acute type, where it is probably the most effective of remedies. Give in doses of a scruple every eight hours, well-diluted to avoid irritating the stomach, and an acute lumbago or torticollis will quickly be assuaged. Otherwise its antineuralgic power, especially marked in the fifth nerve, is due to its action in emptying the bowels and unloading the liver—so frequently the source of these neuralgias.

Ammonium chloride is contraindicated by gastric or intestinal inflammation, severe dyspepsia, marked emaciation or wasting disease, and by anemia unless dependent on fecal retention and autotoxemia. It aggravates the hyperemic stages of acute respiratory catarrhs. As an expectorant it ranks with sanguinarine, scillitin and senegin, and is suited to cases with plethora, or those whose lymphatics are loaded with debris.

It is antagonized by the sedative expectorants, and in some ways by the general circulatory depressants. It is incompatible with the alkalies, alkaline earths and their carbonates, tartaric acid, mineral acids, and the soluble lead and silver salts.

The dose as an expectorant is 1-6 to 1 grain, well diluted, every hour. To act on the liver give 5 to 10 grains at bedtime.

ANEMONIN

Standard granule—Anemonin, true, gr. 1-134, Gm. .0005, equal to about 1 m. of a standard tincture of pulsatilla.

Anemonin is the active principle of Anemone pulsatilla and A. pratense. Unless the plants are collected soon after flowering the product is not very active.

Anemonin was discovered by Heyer in 1779.

Van Renterghem gives the following process for isolating anemonin: Prepare a very concentrated infusion of anemone in distilled water, and leave to itself for many weeks. It deposits a white substance, that is to be purified by crystallizations in alcohol. This gives an anemonin, white, crystalline, neutral, evaporating at 150 degrees.

Anemonin crystallizes in rhombic crystals and needles, heavier than water. There is little taste to it at first, but a burning sometimes appears later, that lasts for some days. Volatilized by heat, the vapor causes a violent, piercing sensation on the tongue, leaving where it touches numb, white spots. The eyes and nose are irritated by it. It decomposes in air, and in drying. It is found in many species of anemone (ranunculus). It is obtained by distillation with water vapor. It is insoluble in cold water, sparingly soluble in boiling water and in ether, more so in cold alcohol, easily in hot alcohol and in chloroform. It dissolves readily in alkalies, passing into anemonic acid.

Physiologic Action.—Brunton says anemonin may cause local inflammation and gangrene when given subcutaneously, vomiting and purging when given by the stomach. It depresses the circulation, respiration and spinal cord, somewhat resembling

aconitine in its effects. The symptoms are a slow, weak pulse, slow respiration, coldness, paralysis beginning with the legs and extending to the arms, dyspnea, and death without convulsions. Poisoning by pulsatilla is always attended with convulsions, their absence in anemonin poisoning being due to paralysis of the cerebral motor centers, and their occurrence in poisoning by crude plant preparations to the possible presence of another principle that exerts convulsant powers.

Van Renterghem found that it required doses of Gram 0.01 every hour for fifteen hours to produce cognizable effects. These were light prodromes of dyspepsia, anorexia, the sensation of a foreign body in the esophagus that could not be passed on to the stomach; all disappearing by the following morning. The stools were normal, one or two daily, the subject being usually constipated. A single dose of Gram 0.05 produced similar effects. He concludes that in these doses anemonin is not irritant to the stomach or bowels.

Ellingwood states that pulsatilla in toxic doses produces mental hebetude, dilated pupils, coma; it lowers the pulse, vascular tension and heart-force, and causes convulsions. It depresses sensation and motion. In small doses it stimulates the cerebral functions and tones the sympathetic, increases cardiac power and slows the rapid weak pulse of nervous prostration.

Therapeutics.—Anemonin has been given in amenorrhea, dysmenorrhea, bronchitis, and other catarrhs, and in asthma (Brunton).

Borchain recommends it in acute epididymitis. Shapter found it useful in hysteric convulsions, and in reflex uterine spasms.

Phillips speaks of it as useful in mental disorders, and in sudden suppression of the menstrual or the lochial flow.

Bovet considers it a decided sedative in dysmenorrhea.

Ellingwood gives as specific indications for this agent, amenorrhea with mental perturbation and apprehension; spermatorrhea with fear; when genital maladies cause great anxiety. The homeopathists appear to give it whenever the patient is in apprehension of coming disaster. Anemonin gives strength and tone to the reproductive organs, regulating their actions, in the absence of acute hyperemia or inflammation. When this mental state is present during pregnancy, with general lack of tone, anemonin is beneficial; also in nervous exhaustion, nervous headache; the constipation, enuresis and dysuria of hysteria and pregnancy; urinary irregularities of pregnancy with ammoniacal urine, pain, tenesmus, catarrh, burning or shooting pains in the bladder or pelvis; in

leucorrhea with pain in the loins, debility, depression, anorexia and general nervousness; in eruptive fevers, especially measles with excessive mucous irritation.

Scudder gives as specific indications for this remedy: Patient nervous and depressed, cries easily, pulse small and frequent, but soft; extremities cold; menses tardy and scant; patient then uneasy and depressed, with a sense of fullness and weakness in hips and back. It stimulates the mind and the automatic ganglia. Heart symptoms due to apprehension give way to pulsatilla. It relieves the nervous symptoms of the menopause, especially with feeble nutrition present.

Webster credits pulsatilla with a favorable influence over diseased synovial membranes; in crural phlebitis, varicocele, ophthalmia, earache of children (applied locally), "black eye," purpura, tinnitus aurium.

Merrell adds to these indications that of gastric distress after rich, greasy food; gastrointestinal catarrhs, wandering rheumatic pains, urticaria and styes.

As the active agents in pulsatilla are volatile, it is not surprising that preparations made from the dried plant should have proved "inert."

Van Renterghem lists the following affections as benefited by anemonin: Corneal leucoma and albugo, retinal anesthesia, commencing cataract, amblyopia, amaurosis, especially in arthritics or patients with functional abdominal disorders, where anemonin may be given alone or with strychnine; commencing atrophy of the optic nerve. In these ocular affections anemonin may be used locally and internally. Paraplegias relieved by anemonin by Seidler and others, were probably peripheric and diathetic. Clarus reported good results in bronchitis, influenza and whooping-cough, rebellious and irritant cough. Storck advised it to allay inveterate rheumatismal pains; and Von Schroff found it useful in chronic exanthems, serpiginous and syphilitic ulcers.

Merck gives the dose of anemonin as Gram 0.015—0.05 (gr. 1-4 to 3-4), twice daily; maximum daily dose, 0.2 (gr. 3).

Van Renterghem advised doses of Gram 0.001—0.01 every hour.

Chevalier has investigated the active principles of the anemones (*Rev. de Ther.*). Carnivorous animals are very susceptible to the effect of anemone, vomiting following its ingestion speedily. Possibly meat-eaters may prove similarly amenable to its products. Anemonin is slowly absorbed and not very toxic. The symptoms

are similar to those of the plant or the fresh juice, but supervene more slowly. They are, preliminary excitement followed by dyspnea, motor and sensory paralysis, convulsions, and death. Ballon found anemonin a valuable analgesic, acting especially on the sympathetic nerve; almost specific in oophoritis, orchitis, dysmenorrhea, all genital inflammations in either sex; also in whooping-cough, asthma, and hay-fever. The dose is from 5-6 to 3 grains. A one-percent alcoholic solution applied to the skin vesicates.

Felter and Lloyd say that pulsatilla especially strengthens sympathetic innervation, very markedly in the troubles of the reproductive organs of either sex. Scudder used it to allay nervous irritation in weakly persons, affording rest and sleep, avoiding needless waste of nervous energy, and thus aiding the tonic regime. In feeble women and in men who have become nervous from sedentary habits or mental overwork, in the nervous restlessness of masturbators, or those using tobacco to excess, and for nervous women with debility and defective nutrition of the nerve centers, it acted well. The gloomy mentality, disposition to brood, is a condition insisted on by those who prize this agent most highly. This would indicate an action on the intestinal excretory apparatus, which should be sought in the experiments necessitated by the advances made in physiology since the classic work on drug testing was made. "A pulsatilla patient weeps easily, the mind is unsettled, the pulse weak, soft and open, the tissues dry, about the orbits contracted, sunken and dark" (*Lloyd*). It is applicable in insomnia when there is great exhaustion, sleep disturbed by unpleasant dreams, the patient awaking unrefreshed. Other indications enumerated by this authority are: Amenorrhea in nervous anemics with chilliness; menstruation suppressed from cold or emotion; dysmenorrhea not mechanical; leucorrhea with free bland discharge and pain in the loins, in scrofulous cases; in the intermissions of uterine colics but not in the paroxysms; ovaritis and ovaralgia with tense, tearing pain; weak labor pains; pain with debility, even if inflammatory; epididymitis and orchitis, gonorrheal or from mumps—the dark red, congested, enlarged and sensitive testicle indicating it; the pains of orchialgia; mammary swelling metastatic from mumps; it lessens morbid sexual excitement while increasing sexual power; urethral irritation with spermatorrhea and prostatorrhea; nervous irritability with varicocele; chronic gonorrhea with urethral swelling; frequent calls to urinate, dysuria of pregnancy, involuntary micturition from colds or nervousness; frontal headache from nasal catarrh; nervous headache with gastric disturbance and indigestion

of fats; menstrual headache with chilliness and scanty flow; dull, heavy, bilious and gastric headaches; rheumatic or uterine headaches; all headaches relievable by it are anemic—if plethoric they require gelsemium; acute catarrh of the nose, fauces, larynx or bronchi; asthma of pregnancy or suppressed menses; whooping-cough in anemics; stomach cough; the catarrhal symptoms of the exanthemata; the coryza, profuse lachrymation, dry cough and retrocession of measles; irritation of varicella; in cardiac hypertrophy and dilatation, for the nervous apprehension; functional heart affections with giddiness, imperfect voluntary motion, impaired vision, laryngotracheal sensation of pressure with impeded respiration and sense of impending danger; venous congestion short of inflammation, threatened ovaritis, orchitis, varicocele and crural phlebitis; nervousness attending hemorrhoids; indigestion and dyspepsia, constipation in the hysteric (with nux); alternating constipation and diarrhea, with venous congestion; earache from exposure; purulent otitis media and tinnitus; styes; conjunctival hyperemia with weak vision from excess in reading, or sexual; lachrymation from exposure to wind; chronic conjunctivitis with yellow discharge, scrofulous or from exanthemata; ophthalmia neonatorum; deep-seated heavy pain in the eye; lachrymal sac inflammation; rheumatism with shifting pains relieved by cold and worse from heat; to restore milk in nervous, apprehensive women, with painful, swollen breasts. Bloyer advised pulsatilla in jerking or jumping toothaches, and inflammations due to dead teeth.

In this long list the remedy is not advised as a cure for the malady so much as to relieve the nervous apprehension, occurring in weakly, anemic patients. All points to an action on the liver and the bowels.

Writing in 1886, Van Renterghem said that although official in the French Codex, pulsatilla had fallen into complete desuetude by reason of the inconstant and dangerous character of its preparations. It is absolutely necessary to employ the active principle if we desire to utilize this plant in therapeutics. Van Renterghem, as was his custom, tried the effects of anemonin on himself, employing Merck's product. A four-percent alcoholic solution applied to the arm caused vesication in six hours. It is possible that albugo may be cured by the subinflammatory state induced by repeated applications of a watery solution of anemonin to the conjunctiva.

It is significant that nearly every author who has found pulsatilla or anemonin useful has administered it in minute doses.

ANTIMONY ARSENATE

Standard granule—gr. 1-134, Gm. 0.0005

This is a well-defined salt, a chemical union of the two elements. As with all the antimonials in large doses it acts as a depleting agent and emetic. The tolerance of the stomach for this salt is double that it exhibits for other salts of arsenic (Papillaud), and it combines well with alimentation (Burggraeve). In the small and repeated doses of the new therapy it is an excellent expectorant. It prevents or relieves constipation, obviating this effect of iron, and hence is a useful corrigent of the martial preparations. To the blood it gives its vivid color and its avidity for oxygen, as is the case with all arsenical remedies. It is suited to the treatment of dyscrasias and anemias.

Papillaud introduced the arsenate of antimony, recommending it as a remedy in maladies of the heart, in doses of two granules morning and evening, which may be continued indefinitely without harm. Isnard and Jaubert advised it in the neuroses, in maladies of the heart and of the skin, but mainly in asthma and pulmonary emphysema. In obstinate forms of asthma Isnard pushed it to 10 and 20 milligrams a day, with excellent results.

Laura pronounced it a useful special modifier of the bronchial mucosa in mild bronchitis. In the tumultuous heart-action caused by bronchial hyperemias with consecutive catarrh, and in inflammatory affections of the lung, especially in passive engorgements, he found in antimony arsenate great advantages, associating it with nervine modifiers and the well-known cardiants.

The dose varies from 6 to 8 granules a day, the latter being required only exceptionally. If nausea occurs the remedy should be suspended until it ceases. It was once believed that antimony possessed a special control over crescent pulmonic inflammations, and while the remedy has been dropped, the theory has never been disproved. Even so, in acute sthenic pulmonary inflammations we have a double advantage in this salt, as the antimony combats the excessive heart action and relaxes vascular tension, while the arsenic tends to favor quick fatty degeneration of the newly forming exudate, which may thereby be more speedily reabsorbed. Very rarely there is a place for antimony in the early stages of an acutely delirious form of typhoid and other fevers, and quite recently the writer used this remedy in nocturnal paretic delirium.

One of the late Dr. Pepper's favorite prescriptions for insomnia was gr. 1-30 to 1-60 of tartar emetic before each meal; and it often

proved brilliantly successful. The arsenate would be preferable here.

APIOL

Standard granule—Apiol, true, gr. 1-67, Gm. .001.

Green apiol is an oily liquid obtained from the garden parsley, Petroselinum sativum, the yield varying from 1 to 3 percent. It is also found in celery and in Apium graveolens. It is soluble in alcohol and ether; is of a strong odor and sharp, disagreeable taste.

White apiol or "parsley camphor" is a stearoptene, soluble in alcohol, ether and oils. It occurs in long needle crystals of a faint parsley odor. It has been given in malaria and amenorrhea with some success.

The interest in apiol dates from the appearance of Bartholow's book, in which he stated that this substance was an effective emmenagog, which was also safe in case of pregnancy, as it did not cause abortion.

Is it true? For my part I confess that I have never tried it. In these days the evidences of pregnancy are so complete, so easy to elicit, that there is no excuse for a mistake in diagnosis—at least in all the cases that have come under my care a correct diagnosis was possible. And if circumstances arise that render the diagnosis uncertain, there is always the resource of delay till time settles this question.

There is, however, without question a very general belief among practicians, that any active preparation containing apiol is really a dependable remedy in amenorrhea. The marked success of several proprietary articles of this nature must be due to effects obtained from this agent; and clinical experience has proved that apiol has marked emmenagog effects. The effective dose is very large, but even when given during early pregnancy, either by error of diagnosis or with criminal intent, apiol has failed entirely, I have been informed, in emptying the uterus of its undesirable contents. In all cases of menstrual suppression not due to pregnancy, apiol alone or combined with aloin and savine, has proved decidedly effective.

This is the result of an extended quest through the medical literature on the subject of apiol, the results of which are herewith presented.

Physiologic Action.—In doses of gr. 7 1-2 to 15 green apiol produces sensations similar to those of coffee; a sense of strength

and euphoria, and warmth in the stomach. Doses of gr. 30 to 60 cause toxic symptoms, fever, headache, digestive disturbances, vertigo, ringing in the ears, deafness, scintillations, heavy frontal aching, the symptoms resembling those of overdoses of quinine. Apiol is strongly diuretic. In doses of gr. 9 to 12 it causes dicrotic pulse and disorders the rhythm of the heart.

Merck gives the dose of his product as m. 5 to 10 of the green apiol, or for malaria m. 15 to 30; while the dose of the white crystals is gr. 5 three times a day, or up to a dram daily as a maximum.

Shoemaker says parsley is carminative, diuretic, emmenagog, slightly laxative, stimulating to the skin, circulation and bronchial mucous membrane. It contains apiolin, apiin and cariol.

Cariol causes genital hyperemia, increases the urine, causes general tremors or slight convulsions, paresis or motor incoordination, and finally death by asphyxia. In experiments on animals the dorsolumbar cord was much congested, and the uterine vessels engorged.

Apiin acts like cariol on the nervous and circulatory systems, causing a rapid rise of arterial pressure, due to increase of the heart-action and stimulation of the vasomotor centers in the medulla. Both increase the muscular excitability. Apiin congests the uterus and ovaries, and increases the mucous flow. Both are useful in spinal atony.

Apiolin in toxic doses causes somnolence, stupor, paresis, motor incoordination, increased respiration and circulation, and death by asphyxia. Small doses act on the unstriped muscular fiber, especially of the uterus, in pigs causing abortion.

Therapeutics.—Apiol has been used as a diuretic in dropsies, strangury and gonorrhea. It is not equal to quinine in agues. It is used for amenorrhea and dysmenorrhea. It is best suited for the amenorrhea of anemia; and if this is marked, iron may be added with advantage.

King recommends apiol in scarlatinal dropsy, retention of urine; and as a local application for the stings and bites of insects, for bruises, enlarged glands and swollen breasts. When applied directly to the breast or given internally it dries up the milk. He also recommends it for fetid menstruation, neuralgic dysmenorrhea and uterine colic, and for the night-sweats of phthisis.

Homolle and Joret gave apiol in 43 cases of ague, curing 21 cases with one dose, 11 with two doses, 4 with three, 1 with seven, and failing in six cases. Homolle also found apiol useful in neuralgias, dysmenorrhea and amenorrhea.

The apiol of commerce is a mixture of the active principles, of which apiolin is perhaps the most effective. This comes to us from France elegantly prepared in capsules.

I have given apiol and apiolin for amenorrhea and found it effective. In fact, I look upon it as one of the most satisfactory emmenagogs in use, and one singularly free from unpleasant or objectionable qualities. Neither distress nor hemorrhage has ever followed its administration in my hands. I doubt the limitation to anemic cases, and several times have prescribed it for fat, plethoric women, who had every month great difficulty in getting the flow started, and without help would have none, but very marked fullness in the head, with headache, tinnitus, etc. In every case of this description, apiol, in doses of 5 minims three times a day, in capsules, succeeded in inducing the flow within three days, when given at the menstrual period. In one case of this character apiol succeeded after the strongly purgative emmenagog tablets had failed, though purging so severely as to excite hemorrhoids.

In the anemic cases for which apiol is recommended by some authorities, it is not wise to give anything to incite the flow, until by the use of iron, of proper hygiene, and of laxatives usually, the patient has been raised to such affluence of blood as enables her to spare what is required for the monthly loss. Sometimes amenorrhea is a warning from the body that the expenditure is not warranted; though women usually look upon the cessation of the flow as the cause of the ailments that really are the reasons for the discontinuance of the flow. The physician should take time to patiently explain this, as serious harm may result from unwise efforts to compel the flow from an exhausted body.

APOCODEINE HYDROCHLORIDE

Guinard showed first that vomiting did not follow the use of this substance as in the case of apomorphine. Murrell experimented with it and discovered that it was of value as an expectorant. Roviart used it subcutaneously in patients suffering from constipation and reported in its favor. Two cubic centimeters of a 1-percent solution of apocodeine hydrochloride (about 3-8 grain) injected under the skin of a man produced one or two soft motions in an hour. There is no feeling of nausea and a slight irritation at the seat of the injection passes off in a short time.

Experiments on animals go to show that apocodeine acts diametrically opposite to nicotine, that is, it causes vasomotor dila-

tion, fall of blood pressure, increased peristaltic movements. The absence of effect on the stomach by apocodeine may be explained by the fact that the sympathetic gives few if any fibers to the stomach. It can not act centrally on the brain because increased peristalsis can still be seen when the vagi and cord are cut, nor can it act on the extreme periphery, for when applied directly to the living intestine all movements cease. On injecting moderate quantities of this remedy into anesthetized cats and dogs or rabbits, it is easy to show that certain ganglionic cells are paralyzed. After the injection of apocodeine stimulation of the chorda tympani gives no increased submaxillary secretion, although the secretory neurons are active, because the exhibition of pilocarpine still gives rise to a greatly augmented secretion. We infer from this that the ganglionic cells are paralyzed on the chorda tympani.

Experiments with apocodeine hypodermically have been made on an extensive scale by Prof. Combemale, of the University of Lille. In his hands the injection of 30 m. of a 1-percent solution of apocodeine hydrochloride was followed in almost every instance within half an hour by one or two loose stools. The only bad effect he found was some irritation of the skin at the site of the injection, which was avoided by injecting the drug deeply into the muscular tissue.

Apocodeine lowers blood pressure, produces vasodilation, and increases peristaltic movement. This all occurs probably from its sedative action on the sympathetic inhibitory ganglia. It does not produce vomiting, or other ill effects, and merits an extensive trial as a hypodermic purgative. A one- or two-percent solution of the hydrochloride of apocodeine should be used, which solution should be filtered and neutral. Two or three Cc. should be injected for a dose.

APOCYNIN

Standard granule—Gr. 1-12, Gm. .005.

Apocynin is the active principle of the American hemp, Apocynum cannabinum. From another of the Apocyneae, Aescanthera ouabaio, is derived ouabaine, the arrow poison of the Somalis. Apocynin belongs to the digitalis group, possessing their diuretic properties, but differs somewhat in its action on the heart.

This, the only really useful active principle of Apocynum cannabinum (Nat. Ord. Apocynaceae) is obtained from the root of the plant. The popular names of Apocynum are Black Indian

Hemp, and Dogsbane. Besides apocynum, a glycoid, apocynein, soluble in water, has been extracted; but the latter is not used therapeutically. The Eclectics have pushed this remedy to the front and consider it one of the most useful drugs in their list.

Therapeutics.—The information on apocynin we can glean from the standard works upon therapeutics is not startling in its richness.

Shoemaker says apocynum is emeto-cathartic from its apocynein, diuretic from its apocynin. The former is soluble in water, hence the irritating qualities of the decoction. Apocynin is soluble in alcohol, ether and chloroform, but not in water.

Richmond found the plant useful in jaundice and as an expectorant. Glinski found it relieved the functional disturbances attending organic heart-disease and lessened the area of dullness in cardiac dilatation.

Hare advises that if good results do not follow the use of the drug, another sample should be tried; but if you ask him why he doesn't use the active principle and avoid such uncertainty, what will he say? He states that the effects of apocynum in causing profuse diuresis, in cardiac and renal dropsy, have won for this drug the name of the "vegetable trocar."

King says full doses cause vomiting, purging, sweating and diuresis, preceded by somnolence. As a diaphoretic it is of value in malarial fevers and pneumonias.

The decoction is useful in irritation and congestion of the uterus, with nausea, vomiting, tympanites, headache and aortic pulsation. The leading indication is dropsy with debility or struma, but no albuminuria, when it is to be given in small doses to remove the edema, but not as a purge. It acts by restoring cardiac force. If the dropsy is due to organic disease of the heart, liver or kidneys, apocynin will not cure, but mitigates the affection. Nor is it indicated in fever, nor when the pulse is full and hard. Atony is the specific indication, with escape of the blood-serum into the tissues, which become water-soaked. Anemia is also present. It has been used with benefit in acute and chronic hydrocephalus, and in malarial and scarlatinal dropsies. Another action of importance is in amenorrhea, passive menorrhagia and leucorrhea, the uterus large and flabby, its tone relaxed. Edema may coexist elsewhere.

In young girls, where the menstrual flow is too free, comes too often and lasts too long, apocynum is effective. Old scrofulous and syphilitic cases are benefited, which indicates a depurative action. In atonic dyspepsias it removes constipation and fluid accumula-

tions. Rheumatism is benefited by apocynum only if edema is present or the parts are puffy or glistening.

As a heart-tonic, it is useful in dilation of the ventricles, but not when the pulse is hard or quick.

One case was reported in which apocynum benefited an angina with edema. The precordial oppression caused by tobacco was also relieved by this drug. It is most valuable in renal congestion, the second stage of desquamative nephritis. Goss affirmed that it was a useful remedy for ascarides.

Ellingwood says apocynum increases the nervous force and the respiration, as well as the oxidation of the blood. It causes diuresis even when the heart is not affected. It does not irritate the kidneys, but overdoses have occasioned suppression of urine—probably by shutting off the renal arteries. It is of use in acute nephritis, but the inflammation calls for other remedies to be added. He adds iron for anemias. Apocynin controls passive hemorrhages.

The desirable effects of the American hemp are due to the neutral principle apocynin, and a distinct gain is obtained by excluding the irritant emeto-cathartic apocynein. The former has proved a highly reliable diuretic and heart-tonic, closely resembling digitalin in these respects, but differing in that the hemp derivative acts on the liver also, and increases the solid output from this organ and from the kidneys.

The limitation of its use to cases with low vascular tension should be heeded. The best dosage appears to be gr. 1-12 every two hours except when asleep, gradually increased to four times this dose, or until a satisfactory state of vascular tension has been secured. The occurrence of nausea or purging is an indication to moderate the dose.

Webster says that apocynin is a specific for oft-recurring catarrhal attacks limited to the larynx, pharynx and post-nasal region. He speaks also of its use in cases of agonizing pain in the hip or groin, attributed to sciatica, where it afforded prompt relief even when morphine had failed. The same writer values apocynin in the dyspepsias attending diabetes insipidus.

George E. Smith, of Michigan, finds apocynin useful for lameness and soreness of the feet, without obvious cause or general disease.

Apocynin is primarily a vascular tensor, contracting the arteries and the walls of a dilated heart, with an energy closely comparable to that of digitoxin. There is surely peril of cumulation, therefore. In my own use of apocynin I have found the effects

slowly induced but enduring. Beginning with doses of gr. 1-12 every 2 hours, adding this to each dose every day, it is three or four days before irritation of the stomach or diarrhea indicates toxic action, when the dose must be reduced. General anasarca is the indication, and if the intake of fluids is closely limited, apocynin will merit its reputation as the "vegetable trocar." Apocynin stands in a group with digitoxin and scillitin. If either is given in cases of fatty heart it should be with the utmost caution. I consider all three to be contraindicated as a rule in this condition.

Failure will surely occur if the drug is given when the indications are not present; hence apocynin is assuredly not "a remedy for dropsy" in all forms and conditions.

APOMORPHINE

Standard granule—Gr. 1-67, Gm. .001.

Apomorphine is an artificial or synthetic alkaloid, prepared by heating in a glass tube at 301° F., one part of morphine and twenty parts of pure hydrochloric acid. One molecule of water is lost. This product, after passing through several purifying processes, is finally crystallized as apomorphine hydrochlorate. It contains none of the anodyne properties of morphine, but is one of the most prompt and unirritating emetics we possess. It is not excreted into the stomach like morphine, and may be decomposed in the body.

Apomorphine hydrochlorate forms small, white or grayish crystals, soluble in six to eight parts of water, or fifty of alcohol, but not in ether or chloroform. Treated with nitric acid it forms a blood-red solution; with an excess of caustic soda, a purple or dark solution. The fresh watery solution is nearly or quite colorless. It must give no color, also, with ether.

Physiologic Action.—Apomorphine is a true physiological emetic—that is, it acts upon the vomiting center to produce emesis and not as a local irritant in the stomach. For this reason it is our safest reliance as the first step in the treatment of cases of poisoning, because it can be administered hypodermically even when the patient is unable to swallow an ordinary emetic.

Except in cases where there is an idiosyncrasy towards the drug, which are not of frequent occurrence, no depression usually follows its administration. If larger doses than are really necessary be given, the symptoms may reach the degree of collapse, especially in children. But, in proper dosage very little nausea accompanies the emesis, and the contents of the stomach are thrown off with a

few efforts. And, in spite of a few cases on record where serious effects have resulted from its administration, apomorphine is regarded, when injected hypodermically, as a safe, prompt emetic.

Nichols says that its operation does not result from elimination through the gastric mucous membrane, since intravenous injection is followed by emesis in animals whose aortæ have been previously ligated, thus preventing any of the apomorphine from reaching the stomach.

Rossbach in 1882 demonstrated the secretory stimulant action of apomorphine. The mucus secreted resembles serum. The muciparous glands are hypertrophied. The increase of secretion does not depend on hyperemia, nor on a central excitation of the gland cells, but on a direct action on the glands or on the peripheral extremities of the secretory nerves, or on their ganglia.

Emetine is a synergist, and both as an emetic and expectorant replaces apomorphine in most cases. During infancy and when the stomach cannot be used, as in trismus and in mental maladies, the preference is for apomorphine; also when special precautions must be exercised to preserve the gastric mucosa and its functions free from irritation. Pilocarpine presents some analogy of action, as it also increases bronchial secretion and occasionally induces vomiting; but its sweating and salivation are peculiar to it, and more decided than those following apomorphine. Huesemann found that chloral and morphine suspended the action of apomorphine, which will not act as emetic in narcotic poisoning. Atropine and hyoscyamine are more directly antagonistic, as they check mucous secretion and quiet vomiting by sedating the muscular fibers; still the emetic action in full doses will occur despite these. Von Gellhorn recommended apomorphine as a calmant and soporific in acute mania. Muennich used it in spasm of the glottis; Vollender to cut the epileptic paroxysm. Van Renterghem limits its uses to those of an emetic and expectorant. It is of value when it is desirable to empty the stomach when overloaded with food and alcohol, also to rid the bronchi of secretions, the larynx of false membranes, foreign bodies, etc. Rossbach praised its action in croup, and in chronic respiratory catarrhs. In whooping-cough Van Renterghem gave it with hyoscyamine, calcium sulphide, brucine, and quinine hydroferrocyanide. Hyoscyamine acts as an antispasmodic, apomorphine thins the secretion, calcium sulphide destroys the parasites, quinine combats fever, and brucine sustains the vitality. The change in color does not indicate an alteration of the composition or the action of the medicament.

If given by the mouth in similar doses, according to Murrell, apomorphine does not even cause nausea, but powerfully stimulates the secretion of the respiratory mucous membrane. Rossbach states that non-emetic doses promote the excretion of mucus and make it more fluid. This will be further considered under the therapeutics of the drug. Cushny claims, however, that this is simply the beginning of the nauseant action that leads to vomiting.

Locally, apomorphine solution anesthetizes the cornea, causing dimness of vision. As with morphine, a feeling of well-being—euphoria—lassitude or somnolence, may follow the primary effect of apomorphine, whether emetic or expectorant.

Toxic doses paralyze the emetic center and narcosis ensues, with abolition of reflexes and dilatation of the pupil.

Nervous irritation, hyperesthesia, depression of the circulation, shallow, irregular respiration, convulsions and collapse have been noted. (*Nat. Stand. Disp.*)

Liebreich says apomorphine has no influence on the striated muscles, the motor, sensory or vasomotor nerves of mammals. Reichert, however, showed that toxic doses lower arterial pressure, following a distinct rise, which is prevented by previous section of the cord, and is therefore due to stimulation of the vasomotor centers. He also showed that apomorphine is a muscle-poison (*Wood*).

Doses of gr. 1-20 hypodermically injected induce vomiting in twenty minutes; gr. 1-10 in ten minutes; gr. 0.45 in two minutes, repeated within half an hour (*Bourgeois*).

Therapeutics.—Apomorphine is the only emetic we possess for hypodermic use, and is of value in cases where quick, safe and sure emesis, with the minimum of nausea, is necessary. Its chief advantage, therefore, is in cases of narcotic poisoning, where lethal doses have been taken, resulting in coma with loss of the ability to swallow any of the usual emetics; and prompt emesis must be obtained if the patient is to be saved. Here, the hypodermic administration of apomorphine is often a life-saver.

In cases of attempted suicide, where the person refuses to take an antidote, apomorphine may be successful in saving a life because of its action upon the vomiting center, following subcutaneous injection.

A few tablets of apomorphine should be carried in the hypodermic case as a matter of routine, particularly by physicians whose practice is in localities removed from sources of supply.

The dose as a prompt emetic in emergency cases is usually gr. 1-10, hypodermically injected.

In severe spasm this drug has given good results, even in children, and J. S. Horsley reports a case of strychnine poisoning as controlled by apomorphine, which eventually recovered entirely. In cases of threatened delirium tremens, when the patient is in a condition of muscular and mental excitement, gr. 1-10 of apomorphine usually relaxes the entire system, produces calm and frequently the desired sleep. The dose may be repeated every half-hour until effect; the amount varying in different individuals.

In that form of hysteria whose dominant symptoms consist in clenching the fists, kicking the feet about, staring eyes and closed lips, but without any apparent reason—and whose fundamental causation might be aptly, though, I confess, not elegantly expressed, as "cussedness"—a hypodermic of apomorphine will work a marvelous and salutary change in a reasonably speedy and benign manner.

Vallender found it useful in epilepsy.

Sleep has followed its nauseant action in the insane.

Apomorphine is not only a valuable emetic but it is also a most efficient expectorant. In small doses, gr. 1-67, frequently repeated, it increases the secretions of the mucous membrane of the respiratory tract. It is the remedy, therefore, when there is dryness and deficient secretion, tight cough and tough sputum. In acute laryngitis and capillary bronchitis it has proven of great value from the fact that it seems to be a *mucus attenuator* as well as a stimulator of the membrane. The dose should be small and frequently repeated.

The solution containing apomorphine, on standing for a short time, gradually turns gray, then green, and although some writers on materia medica declare this color-change produces, in some way, a change in the character of the drug that makes it dangerous to use, the writer has used it in the above way time and time again without being able to notice any difference in the action of the apomorphine; certainly nothing deleterious. In fact Harnack and Hildebrandt (*Munch. Med. Woch.*, 1910, page 20), insist in a study on apomorphine that this color change is necessary, and they claim that an apomorphine solution which on standing does not soon turn distinctly green should be rejected. It is possible that those writers on materia medica who still, with infantile precaution, declare that "aconitine is too active a poison for internal use," may also tremble at the color-change produced by oxidation in a solution of apomorphine and water, but we assure our readers that it is quite uncalled for. A small amount of hydrochloric acid added to the solution clears it at once, and removes the green tint almost instantaneously.

In capillary bronchitis the tendency to carbonic-acid poisoning and subsequent paralysis is well known and dreaded. By the early use of apomorphine combined with strychnine we produce a *thinning of the mucus* in the bronchioles (which are liable to become plugged up with a tenacious exudate), thus anticipating a condition of occlusion in the alveoli which is the alarming feature of this disease. In the meantime the strychnine supports the nerve-centers against the collapse of the patient, and greatly assists in the removal, by expectoration, of the accumulating exudate. It should be given early in the disease and in this way may prevent disastrous results.

If there is fever present, as there frequently is, the addition of aconitine, gr. 1-134, with each dose, is indicated. For the irritation of coughing, codeine is the best remedy, in combination with the above; and if the cough is of the spasmodic type, a granule of hyoscyamine, gr. 1-250, may be added with advantage.

In narcotic poisoning the depression of the medullary centers may be too great to allow the action of apomorphine; when the stomach should be washed out. Or if the patient can be made to swallow, a seidlitz powder should be given, first the contents of the blue paper in solution being swallowed, and then the contents of the white paper, also in solution. Effervescence occurs in the stomach, giving the most prompt emetic effect producible, without the slightest nausea or symptom of collapse.

All emetics are contraindicated in corrosive or irritant poisoning: in atheroma; fatty or dilated heart or aneurism, where a sudden rise of blood pressure is dangerous; also in advanced pregnancy, reducible hernia, gastric or intestinal ulcer, impacted gallstone, abdominal abscess, or whenever sudden strain may do harm.

Murrell believes the difference in the effect of apomorphine when administered hypodermically or otherwise, is simply due to the rate of absorption. He found this salt could be applied to the skin as an ointment, in doses of 0.01—0.07 (gr. 1-6 to 1), well rubbed in, when it acted as an expectorant, inducing no nausea. This is a valuable method of treating children.

Brunton advises morphine and apomorphine given together for cough, to increase mucous secretion and lessen irritability of the respiratory center; especially when there is dyspnea, constant cough and the secretion of tough mucus.

Murrell advises apomorphine in a spray, as an expectorant, using half a dram of a one-percent solution, if needed.

Shoemaker mentions the use of apomorphine as a remedy for spasmodic croup, asthma, convulsions, strychnine poisoning, mani-

acal delirium, and to relax rigidity of the os uteri. He states that this drug should not be continued too long, as it is liable to produce pulmonary edema.

Harnack and Hildebrandt have ascertained that there are several apomorphines which are chemically very similar but which differ in one point hitherto unknown. (*Therapeutische Monatshefte*, 1910, page 99). Qualitatively the various apomorphines show the same paralyzing effect upon the central nervous system and upon the striated muscles of frogs, but this effect differs quantitatively. Amorphous apomorphines, moreover, show considerable qualitative differences in warm-blooded animals. So does the dibenzoylapomorphine not act as an emetic, and Bergell and Pschorr claim that the specific emetic effect occurs only when the two phenol hydroxyls are present as constituents.

The euporphine marketed by J. D. Riedel is a bromide of methyl apomorphine, and contains from six to eight percent. of apomorphine, which is claimed to exclude the remedy from clinical administration. Euporphine freed from its admixture of apomorphine exerts in dogs an emetic effect if given in doses fifty times larger than that of apomorphine. Experiments on its action as an expectorant, which had been commenced in the medical clinic in Halle, were not encouraging, and any action which it possessed must be attributed to its apomorphine content. This experience shows that the attempts at preparing "improved" apomorphines are idle.

The dose of apomorphine, as an expectorant for adults, is three or four granules every half-hour or hour. For a child of four to six years dissolve 24 granules in three ounces (twenty-four teaspoonfuls) of water; a child of two years, 20 granules in three ounces of water; a child of one year, 15 granules in three ounces of water. The dose is a teaspoonful every fifteen to sixty minutes. An infant may receive half a teaspoonful of the solution prepared for a child one year old.

In any case, if improvement does not follow within three or four hours, the dose should be increased.

The drug should be given with the care due when any depressing remedy is administered. The antidote, in cases of poisoning, is strychnine hypodermically, caffeine hypodermically, or hot coffee internally with applications of external heat; or all together if the case is urgent.

Apomorphine antidotes chloral and chloroform, being their physiologic opponent. It is incompatible, chemically, with alkalies, potassium iodide, and iron chloride.

Laura found that apomorphine slightly lowered the body temperature, at first excited and then depressed the action of the heart, augmented the number of the respiratory movements, increased nearly all the secretions, such as the saliva, tears, intestinal juice, and was probably eliminated by all routes.

Verger employed the emetic power of apomorphine to dislodge the stone of a plum lodged in the esophagus of a little girl. Jurasz found this agent serviceable in the treatment of tracheitis, bronchitis of the large and the small tubes, the râles becoming humid and expectoration easier. Ruatta vaunts it in hysteria, where its utility is explained by the powerful concussion given to the nerves. Laura suggests that in neuropathies in general such remedies act dynamically, by altering the irregular nervous impulse and reestablishing the lost equilibrium by the new impressions and modifications induced.

ARBUTIN

Standard granules—Gr. 1-6, Gm. .01; gr. 1-67, Gm. .001.

Arbutin is a glucoside obtained from uva ursi, gaultheria procumbens, pipsissewa, and other species of arbutus. It occurs in silky, needle-like crystals, soluble in boiling water and in alcohol, slightly in cold water. It is bitter, and the solution does not ferment with yeast. With iron chloride it gives a blue color. It is mostly excreted unchanged in the urine in a short time, a little being excreted in the urine as hydroquinone sulphuric acid. Lewin thinks the formation of hydroquinone may cause therapeutic effects in the urinary tract. Mencke hoped that arbutin might cure gonorrhea through the formation of free hydroquinone, but this was disproved by Paschkis.

Arbutin is undoubtedly the principle to which these plants owe chiefly their activity. It is stimulating to the renal cells, and mildly antiseptic. In large doses uva ursi causes vomiting and diarrhea, but arbutin does not have this effect. The leaves of uva ursi contain 3.5 percent of arbutin and 34 percent of tannic acid. Thus, in using the leaves to obtain 15 grains of arbutin, a full dose, one must take about 150 grains of tannic acid, besides enough woody fiber and other useless matter to make the dose up to an ounce.

Physiologic Action.—Brunton ranks arbutin among the astringents, coagulating albumin and constringing the cells, not the blood-vessels. It diminishes the exudation of albumin through the Malpighian tufts, more powerfully than tannic acid Its specific value is in catarrhs of the bladder and the genitourinary passages.

Hughes found arbutin a powerful diuretic in doses of one grain. It is not toxic, as Jablonowski took within forty-eight hours 20 Grams of it without discomfort. Though Brunton has shown that arbutin is more powerful than tannic acid, Wood still asserts that the latter supplies the chief value to uva ursi.

Therapeutics.—The specific indication for arbutin is atony or hypersecretion of the uropoietic mucosa. Introduced subcutaneously or by the mouth, arbutin is eliminated by the kidneys. It combats putridity and sepsis, acting alike on the tissues of mucous cavities and the urine contained. It is useful in acute or chronic cystitis, pyelitis, pyelonephritis, gonorrhea and leucorrhea. It corrects putrid fermentation of the urine with ammoniacal odor.

Ungar reported the case of a man, 68 years of age, with hypertrophied prostate, who had been compelled to use the catheter since 1875, occasioning an obstinate cystitis. Urination was almost constant, the urine fetid and ammoniacal, in spite of intravesical washings with carbolic solutions one-half percent, twice a day, with salicylic acid by the mouth. In 1879 grave hematuria appeared, repeated until 1883 at least weekly, lasting several days each time. Near the end of 1884 all other medication was discontinued and arbutin alone given for four days, in doses of Gram 0.5, t. i. d., then Gram 1.0 t. i. d., for three doses. The effect was very good. For some weeks the urine was free from pus and mucus, the bad odor disappeared, the hemorrhage ceased, the general health improved and the continual tenesmus subsided. Had not the continued use of the catheter reproduced the malady, a complete cure would have been obtained. The patient, taking still two daily doses of Gram 0.5 each, had not presented any therapeutic accident whatever.

Gris cites a case of pyelitis cured by Guyon by means of arbutin, and says he could cite other cases.

Viriate Brandao reported three cases of cystitis cured by arbutin, and declared that its use superseded the need of other remedies, sandal, balsams, etc. Hughes and Menches also made favorable reports on this remedy in cystitis.

Ferran lauds arbutin, in his work on the maladies of old age.

While large doses are not toxic they are largely wasted, if they are right who attribute the whole effect of arbutin to the minute quantity that goes to form hydroquinone. This I believe to be a mistake; and that the undecomposed arbutin itself is the principal remedial agency. This is shown by the decided curative results following the use of very large doses, as herein detailed. The doses

should be repeated often—every hour or two—on account of the rapidity of elimination.

Houdé recommends Gram 0.04—0.08 every hour by day, and each time the patient rises at night to urinate. The daily dose should be from Gram 0.6 to 0.2; or enough to stop urinary putridity.

Van Renterghem took in one day a Gram of Merck's crystallized arbutin without experiencing any notable effects (in health). He recommends the administration of this agent every half-hour, to insure its continuous, uninterrupted influence; in doses of Gram 0.01—0.02. He reports the case of a girl, aged 22, ill six months, menses stopped during this time, with grave vaginal blennorrhea and subacute vesical catarrh; excessive tenderness to examination, vagina dry, very hot, secreting fetid muco-pus; micturition constant, mucus fetid; sleepless, no fever, appetite and digestion good, stools twice a week, no syphilis.

Treatment. (1) The vagina was irrigated every three hours with warm borated chloral solution, chloral Gram 1.0, borax 0.5, water 1000. (2) Daily enema of magnesium sulphate solution. (3) Hyoscyamine, a granule every fifteen minutes till effect, to relieve vesical tenesmus. (4) Arbutin, Gram 0.04, digitalin, 0.001, every hour from 6 a. m. to 10 p. m.

Reported in one week. Since the second day she could sleep all night, waking only two or three times to urinate; less frequent urination by day; the need of hyoscyamine subsided after the second day. She can now sit down. Genital pains and discharge subsiding, urine more limpid; on the road to recovery. A week later she reported the cure almost completed; she was attending to her housework. At her third visit the cure was found to be complete, and no relapse occurred.

Among the affections for which the arbutin-bearing plants have been recommended are lithemia, gout, rheumatism, dyspepsia, nephritis, hematuria, scrofula, skin diseases, gleet, leucorrhea and ague; as a diuretic in dropsy; in menorrhagia, chronic dysentery, bronchorrhea, diabetes; as a substitute for ergot to cause uterine contractions; and in enuresis.

In desquamative nephritis, when the loss of albumin is sufficient to impair the patient's strength, this loss may be checked by arbutin. It is also believed that the persistent use of this agent, in moderate doses, a grain a day, divided, for months, tends to restore the affected tissues to a healthy state; if the diet and general hygiene be regulated at the same time. In cases of enuresis dependent on hyperesthesia of the bladder or urethra a like use of arbutin has succeeded

in gradually restoring normal conditions and function. As with so many of our plant remedies, arbutin is most valuable when given for prolonged periods, even for a year, the improvement resulting quite slowly.

It is obvious that the substitution of arbutin for the plants containing it opens up a new era in the treatment of genitourinary catarrhs. The enormous quantity of tannic acid and of woody constituents necessarily taken with the ordinary preparations of these plants, disguised the effects of arbutin, caused gastric and intestinal distress, and sadly interfered with the absorption of the arbutin. Besides, very little of this agent is present in watery preparations, unless taken quite hot. For these reasons uva ursi and its congeners, while acknowledged to possess a specific beneficial action upon catarrhal affections of the urinary passages, were rated as uncertain, feeble and ineffective remedies, and were prescribed as adjuvants or placeboes, with little expectation of benefit. Under the circumstances it seems surprising that they were retained in the official pharmacopeias—possibly the lack of anything better explains their retention.

But with the production of arbutin in a state of purity all this is changed. We have here an agent of unquestionable and remarkable power, with properties sharply differentiated from the tannin group of astringents. Indeed, to one who is familiar with the properties of arbutin, Wood's assumption that it is the tannic-acid group to which uva ursi owes its effects, can only provoke a smile.

Arbutin is a tonic to the urinary mucosa, correcting relaxation, checking the discharge alike of albumin, pus, blood and mucus; and tending to restore the mucous membrane to a normal state. It is alike beneficial in gonorrheal and other catarrhs, acute and chronic. It is of especial benefit when the urine is fetid and ammoniacal. In the vesical ailments of old men, with dribbling, frequent micturition, the calls to urinate being so imperative that the victim cannot get to the closet quick enough, but soils his clothes, arbutin is a remedy whose value will be manifested whenever it is used.

Secondarily, it is beneficial in atonic dyspepsia, which so frequently accompanies the urinary maladies of old men. This combination of properties places arbutin in the very front rank of remedies for this class of ailments, with no rival.

In acute affections, and in catheter cystitis with fetid, ammoniacal urine, it should be given in full dosage, up to a Gram or more daily. In all cases Van Renterghem's advice should be followed,

and the doses given every half-hour to insure a continuous action. In chronic cases it may be given in increasing doses, beginning with Gram 0.01 every half to one hour, increasing until the urine is free from turbidity or blood, and then in sufficient doses to keep it clear.

The darkening of the urine from arbutin must not be mistaken for that caused by overdoses of carbolic compounds like salol. The latter breaks up the red blood corpuscles, causing hemoglobinuria, a dangerous toxic symptom; while the dark color of the urine from arbutin is due to hydroquinone and is not a toxic symptom. For this reason salol and arbutin, both useful in cystitis, should not be given together.

Nuyar places the daily dose in gonorrheal cystitis at 24 1-2 to 45 grains of pure arbutin. Such doses are only suitable to old and obstinate cases.

W. M. Barnes, of New Jersey, reports a case of chronic nephritis and enterocolitis, in which a cure was effected by the use of arbutin. In another case similar benefit was obtained from arbutin and calcium sulphide. The same physician reports excellent results from arbutin in cases of catarrh of the bladder.

Remedies adjuvant to arbutin are, cubebin and piperine, as mucous stimulants; strychnine and quinine as tonics and tissue contractors; digitalin as diuretic and antiphlogistic; hyoscyamine and atropine as relaxants of the sphincters; cicutine and codeine as general analgesants; cocaine as a local anesthetic.

Houdé says: "In three great varieties of renoarterial infection the kidney is not increased in size. In the last variety we have to deal either with a simple pyelitis or with a pyelonephritis, which is an infection of little severity on the border between medicine and surgery. Later on the suppuration increases and so does the volume of the kidney, and then we have a pyonephritic sac, and the kidney is no more than a shell without parenchyma and full of pus. In case of tuberculosis we operate at present before it comes to this stage, at the period of granulation or of caseous cavities opening into the renal pelvis.

"It is very important here to recognize the character of the pus. In the kidneys of aged urinary pyelitic patients there is troublesome polyuria with turbid pale urine, without chromogene, and a low rate of urea and chlorides, showing a weak organic metabolism. These are patients of feeble vital resistance.

"On the contrary in stout patients with pyelonephritis or pyonephritis we may at times see greenish, dense and concrete pus

precipitated to the bottom of the urinary vessel, two or three fingers' thickness, and mixing with the urine with difficulty.

"The histologic examination of these urines is of interest, especially for those who investigate specific elements, e. g. casts in lesions of the parenchyma, spindle-shaped cells (*cellules en raquettes*) from a suppurating renal pelvis, the bacillus of Koch, and the presence of erythrocytes in tuberculous suppuration.

"As to albumin it must be carefully noticed that it is present in all pyuria, but only in small quantity, some centigrams or rarely some grams per liter, and the interest is to find out whether the albumin comes from the pus and not from an essential renal albuminuria necessitating a milk diet. It is on this account that the physician must submit the urine to a chemist for a complete chemic and microscopic examination, as only an expert can determine the presence of tuberculosis, and the physician must be sure of this, so that he would not condemn the unfortunate tuberculous patient to an exclusive milk diet who is rather in need of superalimentation.

"All these questions in renal suppuration are of great importance where we have to ascertain whether we have a common or a tuberculous suppuration before us, for in a great majority of these cases the welfare of the patient depends upon a well-applied therapy.

"From the above rapid review the physician can learn of the variety of causes, all of which tend to a pyuric syndrome, and it should give him a clearness in making a diagnosis as to its locality in the different segments of the urinary apparatus.

In most cases which we reviewed, even those which at first sight seem to belong solely to surgery, even in these the physician should, before adopting extreme measures, always try the remarkable action of arbutin.

"The first experience of him that resorts to the use of arbutin is that it is non-toxic. It has no bad action on the digestive tract, whatever the dose.

"By its decomposition within the system into hydroquinone it possesses remarkable antiseptic, antiputridic and antizymotic properties, while it is diuretic at the same time. As its elimination is principally by the urine it naturally exercises its special antiputridic and antiseptic action on the kidneys and bladder.

"The action of arbutin resulting, as it does, from its decomposing into hydroquinone, one might ask, why not give hydroquinone directly? But this does not hold good, for arbutin owes its efficacy to its being decomposed, as Sendin showed, within the body. The

soluble arbutin acts only by its splitting in the presence of dilute acids, or in an emulsion of hydroquinone (Hlasiwez and Haberman).

"It is shown that splitting takes place in the bladder (Dr. Landin), and is non-toxic, for two reasons: (1) Arbutin holds but very little of it; and (2) hydroquinone changes in the kidneys and bladder into hydroquinone-sulphuric acid which is inactive.

"It is for this reason that even a small dose of arbutin is sufficient to keep up in the bladder continually this invaluable hydrochemic splitting, the continual contact of which with the mucosa of the sick organ must be of supreme value in the therapy of the urinary passages. Strong doses are not necessary and small doses of the remedy frequently repeated every hour or two keep up its beneficial action."

Houdé's dose for twenty-four hours will vary from Gram 0.60 to 1.20 (gr. 9 to gr. 18); small doses may not show the antiputridic effects sufficiently, especially in severe cases, and large doses of Gram 1.20 (gr. 18) are useless but not dangerous.

ARECOLINE

Standard granule—gr. 1-134, Gm. .0005.

All over the world, in the highest grades of civilization and in the lowest savages, we find an almost universal tendency to indulgence in the habitual use of drugs, for the pleasure derivable therefrom, apart from the relief of disease. Few families of the human race are without some form of alcoholic intoxicant. Tobacco had only to be introduced for the craving for it to arise. It is said that the Hottentots of Cape Colony sacrificed for tobacco the herds which alone afforded them security against starvation. Every plant in which caffeine has been found has been adopted as the basis of hot beverages, tea by the Chinese, coffee by the Arabs, chocolate by the Mexicans, guarana by the Brazilian Indians and maté by the Paraguayans. Opium, coca and hashish spread their baleful influence in spite of every consideration against them; while the newer creations of the chemist's art serve as the basis of new and disastrous habituations.

In Eastern Asia immense quantities of the areca nut are consumed as a masticatory, mixed with the leaves of the Piper betel. This is powerfully astringent, and the weak conclusion has been assumed, that the use of this substance is occasioned by the tendency to diarrhea common in hot latitudes. No evidence is offered that the chewing is especially common to those so affected or that it is

in any way a preventive, or is so considered; and as with other habit-drugs we must until better data are obtainable be content with the explanation that men chew betel because they like to do so.

The betel nut is obtained from the Areca catechu, an East Indian palm. Jahns found in it three alkaloids, arecaine, arecoline and traces of a third, probably guvacine.

Arecaine occurs in stable colorless crystals, very soluble in water, in diluted alcohol, less in absolute alcohol, insoluble in ether, chloroform or benzine. It forms soluble salts and has an acid reaction. (Bocquillon-Limousin.)

Jahns considers arecaine the active principle of areca, and pronounces it a powerful tenicide, resembling pelletierine. Half a grain kills a rabbit in a few moments. It resembles muscarine but depresses both respiration and heart, causes tetanic convulsions and increases peristalsis extraordinarily. Locally or internally used, it contracts the pupils. Dose Gram 0.001 (gr. 1-67). (Bocquillon-Limousin.)

Arecoline $C_8\ H_{13},\ NO_2$ is a volatile oil, miscible in all proportions in water, alcohol, ether or chloroform. It forms crystalline salts, and is pronounced very toxic. It exists in the nut in the proportion of about 0.1 per cent.

In doses of Gram 0.025—0.050 hypodermically it killed a large rabbit; Gram 0.020 killed a cat and Gram 0.075 killed a dog. The heart-beats lessened until they ceased, the inspirations being augmented. (Bocquillon-Limousin.)

Arecoline hydrobromate occurs in white crystals, soluble in water and in alcohol. The dose for a horse is given as Gram 0.03—0.06 (gr. 1-2—1).

Physiologic Action and Therapeutics.—Marme says arecoline resembles muscarine in its action on the heart, and depresses respiration. Fohner says arecoline hydrobromate stimulates the salivary glands more powerfully than pilocarpine and is a more active laxative than physostigmine.

It is especially used for colic of horses, in doses of Gram 0.03—0.06; and has been administered to men for tenia, in doses of Gram 0.004—0.006 (gr. 1-15—1-10), and has also been applied locally as a myotic. Dropped in the eye in 1-percent solution it produces violent myosis, reaching its maximum in ten and beginning to subside in thirty minutes (Lavagna). In one and one-half hours the pupil is still somewhat enlarged. Intraocular tension is not modified. Increased refraction from ciliary spasm precedes iris dilation.

In glaucoma Lavagni and Bietti pronounce arecoline superior to physostigmine though less enduring in effect.

Chetwood-Aiken confirms this opinion. No headache or other unpleasant after-effect is noted, as after physostigmine. He uses 1-2-percent solutions. A drop of 1-percent solution instilled into the eye causes lachrymation and ciliary spasm for a minute, slight hyperemia and subcorneal injection subsiding in a few minutes; in two minutes violent clonic spasms of the iris with dilation of the pupils.

The point of especial interest to us is the effect of arecoline in stimulating intestinal peristalsis. If this effect can be produced by doses too small to cause suffering, it is an inestimable remedy; as it can be administered hypodermically. We would suggest that for this purpose a dose of Gram 0.001 (gr. 1-67) be employed and modified according to results. A significant statement in Dr. Thomson's report is that the pain occasioned by a full dose does not last long, but that the cathartic action continues much longer.

ARSENIC

Standard granules—Arsenic bromide, gr. 1-67, Gm. .001; arsenic iodide, gr. 1-67, Gm. .001; arsenic sulphide, gr. 1-67, Gm. .001; arsenous acid, gr. 1-67, Gm. .001; antimony arsenate, gr. 1-67, Gm. .001; caffeine arsenate, gr. 1-67, Gm. .001; copper arsenite, gr. 1-67, Gm. .001; copper arsenite, gr. 1-1000, Gm. .0000625; copper arsenite, gr. 1-250, Gm. .00025; copper arsenite, gr. 1-100, Gm. .0007; iron arsenate, gr. 1-67, Gm. .001; iron arsenate, gr. 1-6, Gm. .01; potassium arsenate, gr. 1-67, Gm. .001; quinine arsenate, gr. 1-67, Gm. .001; quinine arsenate, gr. 1-6, Gm. .01; sodium arsenate, gr. 1-67, Gm. .001; strychnine arsenate, gr. 1-134, Gm. .0005; strychnine arsenate, gr. 1-67, Gm. .001; strychnine arsenate, gr. 1-30, Gm. .002; triple arsenates; triple arsenates, with nuclein.

No remedy has been so persistently advocated, in so many diverse maladies and so extensively administered and lauded as arsenic. And yet, an eminent American writer having challenged the medical profession to produce one solitary instance in which unmistakable benefit had accrued from the use of this medicine, it seemed advisable, that the known facts concerning arsenic be placed fairly before the readers of this work, that they may judge for themselves of the evidence for and against its use.

In the preparation of this paper every accessible source has been drawn upon; and Dr. Epstein has especially searched through the Russian and German works for material. It has been impossible to credit every statement made to its original author, but so far as possible the authority has been given.

Toxicology.—Arsenic is so extensively employed in the arts at present that both the acute and the chronic forms of arsenical

poisoning are common. Arsenic exists in considerable quantities in commercial sulphuric and muriatic acids, and hence enters many drugs and articles of commerce in whose preparation these acids are employed. Toxic effects have been noted from the arsenic in sulphuric acid used in galvanic cells and in that used in preparing glucose, from which poisonous beer has been brewed (Liebreich).

All the medicinal bismuth salts are occasionally contaminated by arsenic, and glycerin containing this impurity has proved toxic. Much damage is done by the arsenic retained by aniline dyes. Scheele's and Schweinfurth's greens are also responsible for many toxic accidents. Not only the greens but many other colors, used in dyeing domestic goods and tinting wall-paper, are arsenical. Wax tapers containing arsenic set free highly poisonous gases during combustion. Rat and fly poisons are general arsenical. Even if the wall-paper showing on the surface is free from arsenic there may be some in the paste or in the old paper underneath.

Velour tapestry, tarlatan, stuffed birds cured with arsenic, artificial flowers and white muslin, have done harm by setting free arsenical dust.

In the arts many cases of poisoning occur from inhalation of arsenureted hydrogen, an unpleasantly smelling and highly dangerous gas.

Arsenic is alike toxic when taken into the body by the stomach or subcutaneously, when inhaled as dust or gas, or when applied to the surface of wounds, from which it is readily absorbed.

Wines have been found to contain arsenic in France. In London milk was found to have been diluted with arsenical water.

There is little uniformity in arsenical poisoning, the symptoms varying with the form in which it is taken, the dose, and especially the solubility. Arsenical gases are most virulent, while the metal itself, unoxidized, is not toxic, a cat having survived a dose of 14 Grams (over 3 drams).

When large doses of arsenic have been taken there may be no symptoms for half an hour or more; then a sense of tightness in the throat comes on, with difficulty in swallowing, gastric uneasiness, followed by gastric pain and cramps, vomiting and purging with rice-water stools later. The symptoms closely resemble those of cholera morbus. Blood appears in the matter vomited, and sometimes in the stools. The urine is diminished or suppressed. With these occur giddiness, headache, cold sweats, pallid, shrunken features, weak, thready, or imperceptible pulse, feeble, sighing respiration, muscular cramps if the loss of fluid is great, and coma

ending in death, sometimes preceded by convulsions (Cushny). The burning pain in the stomach never ceases while consciousness remains. Cramps of the esophagus are frequent. Thirst is violent. The voice is rough and the tongue usually dry, but sometimes salivation occurs. Tenesmus, strangury and hematuria have been observed. The countenance is anxious, the patient restless. The pulse slows as death approaches, and consciousness weakens. These symptoms may continue from a few hours to as many days, according to the dose. If death occurs speedily it is due to the nervous influence and the circulatory effects (Liebreich). If the dose is below the lethal, or is largely vomited, the patient may recover completely or pass into a condition of chronic arsenical poisoning. Sometimes the only symptoms are collapse and coma.

The fatal dose is uncertain. As arsenic is very difficult of solution it is doubtful how much is active at a given time. Recovery has followed the ingestion of very large doses, while Gram 0.1 (gr. 1 1-2) has caused death (Cushny).

Arsenous acid is the most frequent cause of arsenical poisoning.

The first indication is to wash out the stomach repeatedly. Fats lessen the solubility of arsenic and perhaps protect the exposed surfaces and should be given freely. Magnesia has some value as a chemical antidote, but the most highly favored remedy is iron, the freshly precipitated sesquioxide or dialyzed iron. These form a comparatively insoluble compound with arsenic. That it is not wholly insoluble is shown by the therapeutic activity of iron arsenate, hence evacuants should follow the use of the iron. To prepare the hydrated sesquioxide of iron, mix a solution of iron sulphate or chloride with any alkali (soda is best) and strain. An excess of alkali is to be avoided, as this would cause re-solution of the arsenical precipitate. As the quantity of arsenic ingested is rarely known, the antidote should be given profusely, "by handfuls." For the collapse, warmth, caffeine and other stimulants are required.

When the arsenic has entered the circulation, when other forms of arsenic have been given, and when arsenical gases have been inhaled, we are powerless except as to treating the symptoms and sustaining the strength.

Chronic arsenical poisoning may be caused by a single dose, but usually it is due to the continued absorption of small quantities. Brouardel divides the course into four phases:

1. The victim complains of weakness, languor, anorexia, nausea or vomiting, weight and uneasiness in the stomach, diarrhea or constipation.

2. The conjunctivæ are red, the lids itch; coryza, sneezing and coughing occur; the liver may swell, with jaundice; papules, vesicles or erythema appear on the skin, with pigmentation of the skin on the anterior surface of the body from the nipples to the upper thighs and in the axillæ or other parts. There may be brown circumscribed patches. This pigmentation generally disappears when the arsenic is suspended, but may be permanent. In prolonged poisoning the eruptions may resemble almost any skin disease, the hair and nails may fall out, and deep gangrenous ulceration has been observed.

3. Sensation and motion are disturbed, in limited areas, often in the hands and feet. There is intense, persistent headache, or acute pain in knee, ankle or foot, less often in the upper extremity; formication, the pressure of bedding on the legs and feet is uncomfortable; sensory paralysis follows, the sense of touch is weakened, those of cold, heat, and pain increased or lessened. Symptoms closely resembling locomotor ataxia may occur, especially in subacute cases; coordinative disturbances, absence of patellar reflexes, and lightning pains may simulate ataxia.

4. Motor paralysis follows usually in the extensors of the toes, then in the peroneal group; rarely in the flexors of the foot and leg, or the extensors of the hands and fingers. Usually the paralysis is confined to the extremities, but it sometimes extends to the trunk. It is usually symmetrical; the affected muscles atrophy rapidly, and respond slightly to galvanism, but not to faradism except at first. This diminution of excitability may appear before the reaction of degeneration, which then follows. Mechanical stimuli excite the muscles abnormally.

Lead paralysis may be distinguished by the history of prolonged poisoning, the sensory ailments occur later, the forearm is usually first affected, there is the lead line on the gums, and atrophy of the muscles occurs much later.

Arsenical paralysis may appear three days after acute poisoning, but usually occurs later, perhaps not for a month. The sexual function may be stimulated or depressed. In subacute cases the stomach may reject everything swallowed, and great emaciation result. In prolonged cases the victim may sink into an apathetic, demented or epileptic state.

Usually when the poison is withdrawn the symptoms gradually subside, but gastric irritability, contractures, sensory disturbances and paresis may remain. Weak vision, mild optic neuritis and amblyopia have been noted. If degeneration of the muscles has

occurred little improvement is to be expected. Herpes zoster occurs sometimes on the face or on the trunk. Some of the skin affections seen are due to the direct action of the drug; in men handling it the malady first appearing on the hands, is then carried to the nose, arms and genitals. On the genitals a characteristic ulceration sometimes occurs, termed "arsenical chancre." The absence of glandular swelling, the slight hardening and the history, serve to distinguish this from the specific chancre. Blisters, urticaria, eczema and erythema may occur.

The phases of Brouardel are not always distinct, the symptoms of the second sometimes appearing first and those of the others together When arsenic is given medicinally the first symptoms of saturation, or toxic action, are redness, inflammation and itching of the eyelids and conjunctivæ, with dry nose and throat, or coryza. Workmen inhaling arsenical dust suffer bronchial irritation or cutaneous disorders.

Physiologic Action.—In the alimentary canal arsenic produces effects similar to those of corrosives; it, however, does not coagulate, or unite with, albumin. The mucous membrane is red and swollen, the epithelium fatty, sometimes showing ecchymoses. The whole or parts of the gastric mucosa may be affected. If solid arsenic lies long on the membrane, erosions may be formed. From these red lines lead along the sulci where the dissolved arsenic ran. Sometimes the only lesion is a cloudy swelling of the fatty gland-cells.

The bowels present a similar appearance, most marked around Peyer's patches. Even after profuse vomiting and purging small particles of arsenic may be found. The pharynx and œsophagus may be congested. From the stomach downward the changes become less marked, being least in the rectum. The gastric lesions are rarely due to direct contact with the arsenic, and are caused by its excretion, with the aid of the gastric juice (Filehne). The bowels contain the "rice-water" material and necrosed epithelium in profusion.

The liver shows marked parenchymatous turbidity, fatty degeneration and necrotic spots.

Boehm attributes the gastrointestinal lesions to the action of the arsenic causing extreme dilatation of the blood-vessels, with consequent congestion and destruction of the epithelium, and transudation of serum beneath it.

Schmiedeberg thinks that arsenic has a specific action in causing fatty degeneration of the gastrointestinal epithelium. This de-

structive action may be beneficial when present in the mild degree following the use of arsenic in medicinal doses, promoting appetite and digestion. In the spinal cord arsenic induces localized myelitis. The rapid respiration at first, and paralysis of the vasomotor centers, indicate a direct action on the medulla. Tenderness of the nerve-trunks points to peripheral neuritis, and this may ascend to the cord; or, *vice versa* (Cushny).

The pulse is accelerated by small doses and slowed by large ones, inhibition being unaffected. The vascular tension rises at first, falling soon after large doses; the vasomotor centers and later the splanchnic nerves losing control over the vessels (Pistorius).

Sollmann says the marked fall of vascular pressure is almost entirely vascular in origin. Its seat is in the capillaries, whose permeability is increased, as in inflammations. No matter how arsenic is taken the first effect is on the intestines, the capillary paralysis resulting in an exudation raising the epithelium. With small doses this capillary dilatation results in an increase of the nutrition, due to the better blood-supply. It stimulates the bone marrow, increasing the number of erythrocytes; while large doses cause hyaline degeneration and lessen the number of erythrocytes, and the hemoglobin.

When arsenic is injected subcutaneously diarrhea occurs within an hour. Arsenic is stored in all the organs and passes through the placenta to the fetus. The liver does not neutralize or retain it.

The vascular pressure may be restored by stimulating the vasomotor center, but only at first; while splanchnic stimulation still increases the tension. Later, these nerves fail, through paralysis of their ends or of the vessel walls, while other vasoconstrictors can still contract the vessels.

Respiration is hastened at first by small doses, then returns to normal. Later, it ceases before the heart stops from exhaustion and low blood-pressure.

If arsenic is applied to the unbroken skin it is unaffected unless contact is continued, when redness, vesicles, pustules and later violent erythema appear. There is no corrosion, and subcutaneous injections of arsenic are painless. Applied to denuded surfaces or mucous membranes it causes acute pain and slowly destroys the tissues. It acts only on living cells, not on dead tissues. When animals are taking arsenic the epidermis peels off easily (Ringer). This is due to softening of the protoplasm in the deeper epidermal cells (Nunn). Similar changes occur in the eye. The melanosis seems to be due to the deposition of some organic product in the

deeper layers of the corium. Mucous irritations are caused by the excretion of arsenic on their surfaces. Arsenic has been found in the serum of blisters of animals taking the drug (Cushny).

On the blood the action of arsenic is obscure. It lessens the number of red corpuscles, but not the total hemoglobin. In pernicious anemia it increases the number of young red cells while the mature cells are fewer (Engel). Silbermann says it induces wide-spread intravascular coagulation, leading to a fall in blood-pressure and to anemia. Heinz adds that arsenic also induces thrombi of blood-plates, which cause the ecchymoses and ulcers.

Fever is sometimes present in arsenical poisoning, due to the inflammations. Metabolism is affected by arsenic, the nitrogen in the urine is increased, ammonia is augmented and the alkalinity of the blood is reduced by the formation of lactic acid in excess. The glycogen entirely disappears from the liver and is not formed from the food. Puncture of the medulla does not cause glycosuria, though curarine still elicits it. Fatty degeneration of the epithelium is found in the liver, kidney, heart-muscle, blood-vessels, striated muscles and pulmonary alveoli. Necrotic foci are found in the liver with active division of the hepatic cells (Wolkow).

Cushny sums up these effects by stating that arsenic lessens the oxidation of the tissues and causes fatty degeneration of the protoplasm; it may increase the waste of proteids, directly or secondarily to the decrease in oxidation. These effects are simply less in degree than those of phosphorus. Improvement in nutrition from the prolonged use of arsenic in medicinal doses is well attested. Weiske explains this by the theory that more food is digested and less proteid decomposed.

Liebig and Heller thought arsenic acted by depriving the albumin of its sulphur, but Huesemann denied this. The destruction of living tissues submitted to its action is not a simple chemical action. After having impregnated the histologic elements arsenic arrests the vital acts, the metabolism, the interchanges indispensable to their nutrition, and thus provokes escharification and consecutive eliminative inflammation. Antimony and cantharidin, as well as rhus, exert an analogous influence, and they also act only on the living tissues. As arsenic acts only upon living cells, the escharotic action should be greatest on parts where the vitality is least. Its effects are therefore most profound and rapid in the tissues that have the smallest supply of blood, in the epigeneses condemned to premature death, rather than in normal parts. Thus arsenic will follow the cancerous tissue while respecting the normal tissue in

which it is embedded, the *cloisons*, while sulphuric acid destroys everything it touches. In tissues well supplied with blood, the arsenic is carried away before it can accumulate enough to kill the histologic elements. The eschar of arsenic is a sort of mummification, like the cerebral tissues asphyxiated by the plugging of an artery.

While arsenic will not arrest putrefaction, it retards the alcoholic fermentation, but only for some days. Nor are the ferment cellules destroyed by it, but their vitality is impaired and reproduction inhibited.

Some claim that arsenic increases, others that it lessens waste, some that it induces, others that it allays fever. To many it is depressant and paralyzant to the nervous system, to some it is neurosthenic. Much of the contradiction may be explained by failure to distinguish between the effects of small and of large doses. Van Renterghem looks on the action of arsenic as catalytic, exciting the vitality of the blood, which it renders plastic. Very marked is its tonic action upon muscular tissue. Hahnemann found this constrictor effect shown in many ways after death—both orifices of the stomach tightly contracted, also the anal and vesical sphincters, the pharynx, diaphragm and abdominal planes. The common bile duct was so tightly closed that no bile could pass. Burggraeve noted its decided action on the vasomotor nerves, preventing paralysis of the vessels.

Arsenicophagi.—Tolerance is sometimes established when arsenic is taken habitually. The Styrian peasants who eat arsenic believe it enables them to work better, to climb mountains with less effort, especially of the lungs, that it improves their complexions, makes their horses' coats glossy, and the animals stronger and fatter. Arsenic is said to be taken by these men up to 0.5 Gm. (gr. 7 1-2) at a dose, but Murrell puts the maximum daily dose at slightly more than 1-2 grain. These peasants are "said to" live to old age, with no evil results, and to enjoy unusual sexual powers. And on this "say so" is largely based the use of arsenic as a remedy. Experiments on animals have not created toleration but chronic poisoning; and the allegations as to increased endurance of fatigue by arsenic eaters are as yet unproved and contrary to modern scientific observations.

A review of these accounts shows that the good effects are not uniform, but that many die from the drug; that the habit renders its continued use necessary; and that the alleged benefits are no more than could be ascribed to the healthy life of the mountaineer,

whose great respiratory capacity is necessitated by the attenuated atmosphere.

The observations of Schallgruber, von Tschudi and others, of the Styrian arsenic eaters, appear so contradictory to the common experience of the scientific world in general, that some further investigation seems desirable. Gies experimented on animals with the following results:

1. Badly nourished rabbits could not bear the smallest daily doses of arsenic (0.0005—0.002), but became progressively dejected, refused to eat, developed diarrhea, became emaciated, the coat became rough, and the animals died within three and a half weeks. The autopsy showed always catarrh of the stomach with thickened mucosa, fatty liver and other evidences of arsenical poisoning.

2. Young, immature rabbits, pigs and chickens, tolerated the above doses very well, and as shown by comparison with control animals, grew stronger and larger in all ways, more energetic, with finer, sleeker coats, fatter, the bones longer and thicker. Their young also were superior in size, strength of bones and size of thymus, but were born dead—possibly by reason of their abnormal size. But animals kept in cages with those fed on arsenic, or with arsenic scattered under the perforated bottom of the cages, showed the same improvement, though to a less degree.

3. Full-grown rabbits given arsenic acid, 0.0005 Gm. daily for 40 days, did well, fattened, and had a thick layer of arsenic in the cortex of the diaphyses, but not in the epiphyses, where growth had ceased. But the liver, heart and kidneys were fatty (degenerated).

4. None of the animals could be habituated to the higher doses; for when the metal was increased the bone-changes (especially in hens) stopped, and signs of chronic poisoning appeared, emaciation, falling of hair, intense gastrointestinal hyperemia, with violent purging, and extensive fatty degeneration of the heart, liver, kidneys and perhaps the spleen.

Schæfer records thirteen sudden deaths among arsenic eaters in Gratz alone within two years. Toxic symptoms also frequently appeared in persons taking minimal doses.

From the facts Nothnagel concludes that arsenic habituation, even to minimal doses, is by no means a rule without exceptions, and that the physician prescribing this drug should carefully ascertain the patient's resistance to it.

But Knapp produced a man who swallowed at one dose 0.4 (gr. vj) of arsenic acid, with impunity. Hebra gave 0.06 Gm. daily; and Kaposi 22.5 Gm. in a year to one case. However, the

duration of tolerance has not been determined, nor whether death does not finally result from the arsenic. Knapp recovered from the urine of arsenic eaters, 0.032 to 0.029 Gm. of the metal, showing that that quantity traversed the system daily without symptoms of chronic arsenic poisoning.

The residents of Whitbeck, England, use an arsenical water habitually. Beginners experience dryness of the mouth and throat, but this quickly passes off. These people are said to reach old age as a rule; a statement that needs confirmation. While the Styrians are said to take as much as 1.5 grain (Heisch) *per diem*, or once a week perhaps, the Whitbeck people take much less. Arsenic eaters avoid drinking just after taking the poison, and some avoid fats. Some suspend the arsenic and take purgatives at times. The women are said to get fat, with pure complexions and rosy color; but I have never been able to obtain this effect from arsenic. On the contrary, American women who take arsenic become dark, even like the victims of Addison's disease.

The mountaineer believes arsenic improves his lungs, so that he can climb without fatigue or dyspnea. The disuse of the drug is followed by weakness in this respect, which disappears when it is resumed. Whether, however, those who do not use arsenic do not develop equal lung-power, is not settled. It is admitted that arsenic does not always produce the good effects described, and that large doses entail serious inconvenience. Even Tschudi admits that some become sick and marasmic from the drug. Arsenical paralyses are rarely seen.

Excretion.—Arsenic is largely excreted by the kidneys, to a less degree by the gastrointestinal and respiratory mucous membranes, traces being found in the skin, hair and milk. Fatal intoxication occurred in a child whose mother suffered acute arsenical poisoning. Excretion is slow, arsenic being detected in the urine three months after it was last taken. The effects remain long after the drug has been excreted.

Elimination of arsenous acid begins by the kidney in six to eight hours; that of potassium arsenate in one hour. It is also eliminated by the skin, the intestinal mucosa, the bile (Taylor), even by the lungs (Flandin). Chatin detected arsenic in the serum of a blister. Orfila said that elimination was completed in fifteen days; but Maclagan found it required twenty-five days. Accumulation is therefore a probability, especially if the kidneys are diseased. Gubler found arsenic in the urine forty-five days after about eight grains had been taken at one time. The tests thereafter failed to

show the presence of arsenic, but after nine days' treatment with iodides it again appeared. This patient's head was shaved, and in the new growth of hair, eight months after the poisoning, arsenic was found in abundance.

Arsenic is found most largely in the liver; also in the kidneys, stomach, intestines, spleen, lungs, and traces in the muscles and nervous tissues. In the blood it is found in the cells. It has been found in the bones after having disappeared from the other tissues.

As an antiseptic, arsenous acid is one-tenth as strong as corrosive sublimate. The spores of anthrax are destroyed only after ten days' immersion in 1-1000 solution (Koch). It has no action on ferments, moulds and algæ. The bodies of persons dying from arsenical poison are said to remain long undecomposed, but this is disputed.

Binz and Schultz explain the action of arsenic by supposing that arsenous acid is oxidized into arsenic acid in the tissues, and the arsenic acid again reduced to arsenous. Oxygen is thus alternately withdrawn from and again supplied to the protoplasm.

Arsenureted hydrogen is exceedingly poisonous and many fatalities occur from its inhalation in laboratories. It acts as a molecule, AsH_3, arsenites as ions. It destroys the red corpuscles, inducing intense headache, nausea, vomiting, prostration, syncope, cyanosis and collapse. The hemoglobin is reduced. Methemoglobin, hematin and even blood are passed in the urine. Rarely the stools contain blood. The uriniferous tubules may be plugged by debris. Intense jaundice may occur. Death is due to pulmonary edema or to heart-failure. The gas may be excreted by the lungs and is known by the garlic odor. The absorption band of oxyhemoglobin disappears before this is reduced, when further decomposition of the blood takes place (Liebreich).

Therapeutics.—In spite of the very full account given of the effects of arsenic in the human body, we are struck with the fact that scarcely a single therapeutic use of this agent is deducible therefrom. Excepting the possible use of arsenic in diabetes mellitus, and its power of inducing fatty degeneration, we have only the hazardous surmise that, since arsenic physiologically affects certain tissues, such as the skin, it may possibly be found effective in combating pathologic conditions of these tissues. But arsenic acts as a poison, first and last; and the indications for its use are purely empirical. It is questionable whether the constantly recurring advocacy of arsenic as a remedy in all sorts of maladies, especially those usually considered incurable, such as carcinoma and tuber-

culosis, is not due to the somewhat superstitious idea of its powers arising from its alleged use by the Styrian arsenicophagi. This tale seems to have been accepted for generations with very little attempt at verification; and even if these people have acquired a hereditary immunity against arsenic, which has not been claimed, but might be, the experience is altogether exceptional, and nothing like it has been observed in other races and lands. Altogether the tale bears many of the earmarks of a "traveler's yarn," so far as the good effects of the habit are concerned.

In the skin we look for the first evidences of therapeutic action. On syphilitic dermatoses arsenic has no effect. On general eczema, especially the chronic forms, psoriasis, urticaria, lichen, and sometimes on pemphigus, leukemia and pseudoleukemia, arsenic has a beneficial effect. Acne is benefited in proportion as the general health improves, but rosacea is improved or cured. Over lepra, arsenic has no control, nor over furunculosis. The drug should be commenced in minute doses, increased until toxic action begins, when the curative effect should be manifested.

Chronic affections require chronic treatment, and in lichen ruber Hebra gave arsenic for two years.

Malignant lymphoma can be cured by arsenic. During each decade of the last century arsenic was brought forward as a cure for cancer and in each case the claim was disproved (Nothnagel).

Lipp introduced the subcutaneous injection of arsenic in lichen ruber and other dermatoses. The method has value, but fatty liver has developed under it. The injections are apt to cause abscess unless carefully sterilized. Sodium arsenate is preferable for hypodermic use. Little benefit will follow the use of arsenic in skin diseases unless the digestion is carefully regulated.

The salts of arsenic allow a nice discrimination to be shown in selecting each for its proper applications. Burggraeve said: "Quinine arsenate as a corrective of the diatheses in fevers, especially paludal, ranks close to arsenous acid, if not superior to it. It is also excellent in the treatment of pyemic fevers. Strychnine arsenate is very powerful in all cases of respiratory insufficiency, at the debut of pleurisies, pneumonias and cardites, when its employment is urgent, as well as in chronic insufficiencies. The arsenates of iron and antimony suit well in lymphatism, and all maladies dependent thereon, especially maladies of the white tissues. Caffeine arsenate, so useful to sustain the vitality of the heart and the brain, is the sovereign remedy for aconitism, caffeine being a general antidote against excessive doses of any of the alkaloids. Arsenous acid is

a stimulant of the stomach, exercising a beneficial influence over the sanguine crasis, especially in the herpetic and tuberculous dyscrasias, where it is an excellent reconstituent of the blood." This is only true in pathologic states, for in a healthy man it appears to lessen the number of red globules. Arsenic is an aid to combustion, respiratory and nutritive. Whenever hematosis languishes, arsenic establishes it in normal condition. Lee pronounced arsenic almost an alimentary substance, or at least an agent that prevents waste.

Laura recommends arsenous acid in anemias, leukemias and pseudoleukemias. The impunity with which small doses of arsenic may be taken for months he attributes to the fact that it favors the assimilation of albumoses rendering the body stronger and less susceptible to fatigue. It lessens retrograde tissue metamorphosis. It is eliminated by the kidneys and by all the secretions. He finds it also useful in the spasmodic neuroses, epilepsy, chorea, neuralgias, the milder malarial fevers, sexual functional disorders of the female, amenorrhea, dysmenorrhea, leucorrhea, anemia and chlorosis; as a blood reconstituent in palustral diatheses, rebellious fevers with anemia, portal engorgements, hypochondria, in skin diseases dependent on a dyscrasia; in ataxic and adynamic fevers, typhus, typhoid, pernicious cholera and plague. It preserves the tone of the tissues, gives vigor to the body, activates the respiration and all the functions. It prevents paralysis of the vessels, hence its use at the outbreak of all fevers and inflammations.

In *grip* and zymotic fevers, Burggraeve employed strychnine arsenate, with calcium sulphide to clear the bronchi of secretion. Purpura hemorrhagica is but a symptom of the state of the blood and of the vessels; for which we give the arsenates of strychnine, quinine and iron. Arsenic is useful in cardiopathies due to the recession of eruptions. Ringer gave it in irritative dyspepsias and for the vomiting of drunkards. It has been termed "precious" in chronic gastric ulcer and in cancer of the stomach, relieving the pains and stopping the vomiting. Here Burggraeve preferred the arsenate of strychnine, soda or antimony. He used this remedy in nephritis, in the hyperemic stage to reenforce the secretory structure, preventing granular degeneration of the anatomic elements. In zymotic maladies he joined arsenic with the hypophosphites.

Laura says arsenic is well tolerated by infants and of great value in their maladies. Its good effects in all forms of consumption are incontestable (Millot). In albuminuria it has been praised by Jaccoud, Lauder Brunton and Semmola. In diabetes it has

afforded satisfaction with Devergie, Joville, Quinquaud and Bouchardat. Cerisay gave fractional progressive doses in phthisis.

Buchner believed that arsenic renders the body immune against the tubercle bacillus, but this has been disproved. If phthisis is primarily a malnutrition opening the way to the bacillus, it is easy to conclude with Leyden that arsenic can have no effect. Nor does arsenic develop a high state of nutrition, or favor the elimination of microorganisms. Moreover the parasiticide power of arsenic is slight, and it cannot hinder the multiplication of bacteria, nor has it proved effective in lupus, even in toxic doses, where its decided predilection for the skin would render its use *a priori*, advisable. Yet Landerer has obtained good results from subcutaneous injections of arsenic in lupus.

In chronic malaria arsenic has proved undoubtedly a very efficient remedy. After the sequence of chills has been broken by quinine, arsenic may be depended upon to remove the relics of the malady. Iron is usefully conjoined, since anemia is always present as a consequence of the destruction of red blood corpuscles.

Pellagra is controlled by arsenic.

In diabetes arsenic has been employed with varying effect. Arsenic bromide obtained some repute in this affection. The evidence seems to show that arsenic succeeds only in exceptional cases, and as yet the class in which it is best to use it has not been distinguished. The best results have been obtained by giving the bromide in maximum doses for several weeks.

In neuralgia arsenic has been largely used as a remedy for the intervals, in the belief that it exerts a useful influence over the nutrition of the nerve-centers. The fifth cranial nerve has been thought to come most directly under its influence.

Isnard gives arsenic in nearly all purely functional neuroses, especially "general nervousness."

Romberg thinks most benefit is obtained when reflex neuralgia has as its basis uterine or ovarian disease, especially if the patient is anemic, while in plethoric cases the effect may be hurtful.

Chorea usually subsides under the use of arsenic, but this malady usually subsides in six or eight weeks under any treatment. In calisthenics, macrotin, hyoscine and cicutine, with personal and moral hygiene, we have remedies for this affection of more assured value.

In chorea the cause, rheumatism, psychic influence, etc., has no influence on the control exerted by arsenic (Nothnagel).

Tremors connected with centric neuroses, disseminated sclerosis, etc., are amenable to arsenic hypodermically (Eulenberg).

Kuelz and Fuerbringer, after careful experiments, conclude that the apparent benefit from arsenic in diabetes is due to the lessened ingestion of sugar-forming foods, caused by the gastric irritation which is induced by the remedy.

In the form of cardialgia occurring usually at night, without palpable change in the stomach, in middle-aged persons exposed to mental strain, arsenic is the only useful remedy (Leared).

In malignant lymphoma arsenic was used internally and injected into the gland, with a decided decrease of the growth and even a perfect cure (Billroth, Czerny, Winiwarter, Israel, Karewski and Warfingh).

One case of general cutaneous sarcoma was cured by arsenic hypodermically (Koebner).

In pernicious anemia arsenic has been used with asserted benefit, and in leukemia it has been given internally and injected under the skin. Judgment deferred (Nothnagel).

Children bear arsenic relatively well. In old age it easily begets digestive disturbances. It is contraindicated by gastric irritations, and fever, not malarial (Nothnagel).

Séguin advised large dilution with water.

As tonics, the synergists of arsenic are found in iron, manganese, antimony, and especially strychnine and quinine. As opposing the oxidation of the blood, the cyanides aid it; as vasomotor tonics, ergotin and aconitine are synergistic

Romberg found that anemics responded to arsenic better than plethorics. Isnard determined that it could be employed without harm in pregnancy. Buchner advanced it as a specific for tuberculosis. He sought to increase the natural protective forces of the body by exciting a *quasi* inflammatory process around the diseased foci, as the reaction of the animal organism against the invaders. This reaction should be barely perceptible. It could be induced by phosphorus or antimony, but is best elicited by arsenic. Kempner warmly espoused this doctrine, asserting that arsenic always favorably influenced the nutrition and probably jugulated recent tubercular attacks. But Van Renterghem insists that the only value of arsenic in this disease is as a tonic and reconstituent of the blood, a subordinate role to that played by the defervescent alkaloids, etc. Gubler said: "There is a lowering of functional activity in all the great systems, lessening of combustion and of the movement of composition and decomposition, consequent upon the fever. When arsenic is then given the fever subsides, and a possibility of improvement ensues because denutrition is less active."

He believed that arsenic sedated all the phenomena of hematosis, those of respiratory combustion and of pathologic excitation.

As a reconstituent of the blood Malthe found arsenic effective in progressive pernicious anemia, in which he has had many followers. It has proved especially valuable since it has been reinforced by attention to the bowels, the causative influence of fecal toxemia having been recognized. Chiari added his testimony as to the curative influence of arsenic over lymphoma and lymphosarcomas. Gruenmach, Lewandowski and Gueterbock confirmed this claim.

Van Renterghem reported a case of hemoglobinuria, appearing on the tenth day of a bronchopleuropneumonia of unusual severity. Arsenic had been given during the attack, but was stopped, he fearing it might be at fault. The patient grew worse until death seemed imminent, and the use of arsenic was resumed. The results were surprising. Recovery ensued in six weeks, an exanthem showing the beginning of arsenical toxemia.

Salkowsky's experiments induced Leube to apply arsenic in diabetes mellitus, good results following. These were confirmed by Popoff, who noted the disappearance of polyuria and a notable diminution of the glucose. Nothnagel and Rossbach admit the special benefit of the treatment, but deny the permanent cure. Van Renterghem does not look on diabetes as an entity, and insists that the treatment must be suited to the varying conditions presented by the case, and in this view he is supported by Burggraeve.

Isnard obtained fine results from arsenic in the nervous states consecutive to grave maladies, during pregnancy and lactation, and the special neuropathies of puberty and the climacteric. In adynamia, convalescence from acute maladies, at the debut of fevers and inflammation in general, and in fevers of the typhoid type, arsenic acts as a tonic, prevents paralysis of the vasomotor center, and acts on the blood as well.

Trousseau and Germain Sée recommended arsenic in asthma. Huchard employed it frequently with certain success in true angina during the access, and in pseudo-angina to allay the pain. Dujardin-Beaumetz valued it above iron in cardiopathies, especially in mitral affections during compensation. In chronic diseases of the liver and spleen arsenic acts as a deobstruent. Some forms of malaria are more amenable to arsenic than to quinine—such as the quartans, and the irregular and masked forms—while others are better influenced by quinine. It has been claimed that quinine arsenate gives special advantages, one grain equalling in therapeutic value 15 grains of quinine sulphate. Baudin and

other Algerian observers advise the following method of administration:

1. Begin treatment by an emetocathartic.

2. Give arsenic in divided doses, the last one two hours before the expected chill, pushing rapidly to maximal dosage; when the limit of tolerance has been reached lower the daily dose and give part by the rectum. Raise or lower the dose according to the intensity of the disease, and continue arsenic for one or two months to extirpate an old infection.

3. Prescribe a substantial and abundant regime, largely of dark meats, with generous wines (Gubler).

The program found most advantageous in treating our malarias is this:

1. Empty the alimentary canal by repeated doses of calomel and podophyllotoxin, saline laxatives and colonic flushing.

2. Disinfect by the administration of zinc sulphocarbolate, 20 to 40 grains a day, enough to remove all abnormal odor from the stools.

3. Give 15 grains a day of quinine sulphate, or one grain of quinine arsenate, in fractional dosage; so ordered that there shall be at all times a trace of the remedy present in the blood, to act on the parasites as soon as they leave the shelter of the red blood corpuscles.

4. If the liver or spleen is enlarged add a grain of berberine to the daily dose, divided, to contract their structures and force the plasmodia out into the blood-current where they may be met by the germicides.

5. The arsenates of strychnine and iron should be added when their use is indicated; also nuclein to reinforce the phagocytes.

Some begin with small doses and ascend, others follow the contrary plan. When evidences of toxic action begin, the drug must be stopped at once.

The moderate uses of arsenic in small doses may be traced back through all the modern textbooks to Ringer. He advised this agent in several forms of spasmodic sneezing, with itching beginning at one spot in the nasopharyngeal mucous tract, tending to recur more or less constantly on slight provocation. He also advised arsenic for rumination, merycismus or the regurgitation of food without nausea, for chronic bronchitis with free discharge of thin sputa, in non-febrile catarrhs, and the early stages of pulmonary phthisis. In rheumatic gout he employed a bath containing four ounces of washing soda and a scruple of sodium arsenate.

He describes an affection of the tongue in children, a circular rash, beginning at a point, enlarging, with rings coalescing like ringworm, the surface abnormally clean; obstinate and prone to recur, and associated with gastric or intestinal ailments, obstinate diarrhea, or lichen urticatus. In this arsenic proves useful.

In asthma and chronic forms of phthisis he employs cigarettes, made by saturating blotting paper with a solution of fifteen grains of potassium arsenate in an ounce of water. For sloughing of the mucosa of mouth or throat, malignant sores, chronic coryza, any malady alternating with sneezing, and the collapse stage of a choleraic attack, he praises the effect of arsenic. Ringer also recommends arsenic in small doses before meals in anorexia, gastric neuralgia, lienteric diarrhea, irritative dyspepsia, gastralgia, heartburn, the vomiting of drunkards, or of gastric ulcer or cancer. In a large group of nervous maladies this metal has been highly praised; especially in tic douloureux, hemicrania, neurasthenia, angina pectoris, chorea, epilepsy, asthma, whooping-cough, hay-fever; as a rule being best given in the intervals to prevent the recurrence of paroxysms.

Brunton verifies most of Ringer's suggestions, and says that in malaria arsenic sometimes acts better than quinine, and as a rule excels the latter in latent, masked and irregular forms, manifested otherwise than by periodic chills and fever. As a prophylactic against malaria several observers place arsenic above quinine. Brunton strongly urges arsenic in catarrhal pneumonia with delayed resolution. This condition offers a most favorable opportunity for the domiciliation of the tubercle bacillus. Arsenic attacks the consolidation, favoring the occurrence of fatty degeneration, softening and absorption, and hence is prophylactic against tuberculosis. I would advise arsenic iodide for this purpose, pushed until it occasions irritation of the conjunctivæ.

Arsenic is the auxiliary of combustion, respiratory and nutritive (Burggraeve).

Whenever hematosis languishes, it may be reestablished in its normal condition by arsenic (Burggraeve).

Arsenic is almost an alimentary substance, at least an agent that retards waste (Germain Sée).

Arsenic favors the assimilation of albuminoids and in general renders the body stronger and more resistant to fatigue (Laura).

Arsenic lessens the retrograde metamorphosis of the tissues, which makes of it an important compensator of the organic balance (Laura).

In all cases it is less necessary to determine the form than the fundamental nature (*fond*) of the malady, and especially to attack its dynamic and vital element (Burggraeve).

Jaccoud employed arsenous acid in albuminuria, as did Brunton and Semmola; Smith and Spender in chorea; Devergie, Joville, Quinquaud and Bouchardat in diabetes mellitus; Cerisay in phthisis; Cahen in troubles of the great sympathetic; Burggraeve in engorgements of the portal circulation, hypochondria, pernicious fevers, plague, cholera, black vomit, etc.; Black in cholera, Béhier, Fowler and Cantani in rheumatismal arthrites; Lamare-Piquot to oppose a disposition to cerebral apoplexy, and Ruspini in the attack itself; Casali in pellagra; Ruatta in buccal affections of feeble persons, chronic gastric ulcers, and gastralgia with vomiting.

Hunt says arsenic is harmful during the inflammatory stage of eruptions; but Erasmus Wilson gave it in the acute stages of eczema, only using very small doses.

Simpson found arsenic useful in mucous colitis and in membranous dysmenorrhea. In the former malady it has not given me as good results as the silver salts. Murrell alludes to the effects of arsenic given to horses. It makes the coat sleek and smooth, but when the arsenic habit is formed the animals droop and suffer if deprived of it.

Shoemaker pronounces arsenic the only known remedy that has any effect in restraining the development of visceral cancer. Wright regards arsenic bromide as the best remedy against cancer.

Bryan considers arsenic a prophylactic against scarlatina and possibly influenza and diphtheria.

Phillips found it beneficial in scarlatinal albuminuria. It is said to relieve hemorrhoids, and certainly relieves the rectal excoriations common in those subject to acidity and heartburn. Sawyer found arsenic effective in those cases of gastric pain where the taking of food gave temporary relief. Sometimes obstinate forms of syphilis that resist mercury and iodine improve at once where arsenic is added to the foregoing. Drew praised arsenic in splenic leukemia, and Hare advocates it also in leucocythemia and pseudoleukemia, if given persistently up to full tolerance.

It has been advocated in amenorrhea when due to uterine congestion, to anemia or chlorosis. Butler advises arsenic in Hodgkin's disease, melancholy and hypochondria, especially of the aged.

Sympson gave arsenic internally, continued for several weeks, for warts, finding that they gradually disappeared.

Laura believes that arsenic augments the number and the vigor of the blood globules, provokes and perfects the exchanges of metabolism, ameliorates the nutrition and assimilation in the tissues and the organs.

Medicine essays to repair the enormous and dangerous waste of the organic forces exacted by the struggles of modern civilization, by personal and public hygiene; by heroic compensative medicaments, and among these we place in the front rank iron and arsenic.

Arsenic shows its restorative powers to the best advantage when the patient while taking it employs a rich alimentation, analeptic and easy to digest. Devergie asserted that the energy of arsenic was augmented in its salts, especially those of potassium and sodium.

Externally, arsenic is used as an application to cancerous growths. The effect is not due to coagulation but to a devitalizing of the protoplasm. In lupus, by painting with Fowler's solution cicatrization may be produced, but the disease in only veiled.

In the form of Abbott's paste arsenic is employed by dentists to kill the nerve, when the dental pulp is exposed. A bit of the paste the size of a pin-head is introduced in the cavity, first cleaned out and dried with absorbent cotton; then a bit of cotton dipped in damar varnish is inserted to seal the cavity and prevent communication with the fluids of the mouth.

In all external uses of arsenic the danger of poisoning by absorption must be recollected.

Brunton advises a paste of arsenous acid two drams, cinnabar two drams, ashes of old leather eight grains, dragon's blood twelve grains, with water or saliva. Any arsenical paste should contain at least 20 per cent of arsenic in order that the destructive action shall be thorough. A weaker preparation is apt to cause poisoning through absorption taking place before the tissue has been devitalized.

Hebra's paste consists of arsenous acid fifteen grains, cinnabar three grains and an emollient ointment twenty-four grains.

Marsden mixed one ounce each of arsenous acid and acacia, with five drams of water. Of this he painted several coats over epitheliomas, carefully confining it to the growth and covering not over one square inch at once. This is a good rule in all arsenical caustic applications. The sloughing tissue should be removed by poultices. Some cut grooves into the cancerous mass and fill with the paste, leaving it till the tissues are dead. Hue and Paanel injected solutions of 1 to 1000 into inoperable cancers.

Manec's paste consists of fifteen grains arsenous acid, seventy-five grains of black mercury sulphide and thirty-five grains of burnt sponge; but this seems too weak for safety.

Orpiment, an arsenical ore, is sometimes used as a depilatory; one part with five of slacked lime forming "Rusma Turcarum;" and five parts orpiment, fifty of slacked lime and thirty of starch, forming Plenck's depilatory. The latter is to be kept in a well-stoppered bottle to exclude air. A little is moistened, made into a thick paste and applied to the hairy parts for a short time, then scraped off with a dull knife.

Ringer painted corns and warts with Fowler's solution; but as to corns I must warn against the use of every species of caustic.

Arsenical solutions to be kept free from algæ should have a little alcohol added. Hypodermics for lymphomas should be injected into the substance of the tumor. The internal administration, however, answers quite as well. Do not stop arsenic when evidences of toxic action are manifest, but diminish the daily dose until they cease. So, also, when a cure is evident, reduce the remedy gradually, increasing the doses if a relapse occurs. Otherwise a perilous fall in vitality, or emaciation, may ensue. Acute cases do not require large doses pushed to the verge of toleration, but small, frequently-repeated doses.

In administering arsenic, whenever the effect desired is allaying pain or irritability of the stomach, the dose should be very small and administered when the stomach is empty. If it be desired to obtain the full constitutional effect, as in combating malaria or an inveterate neurosis, it is usually recommended to give the remedy after meals and push to full toleration. This is based on the belief that the large dose unites with the food and is absorbed in some unknown, non-irritant form. Were this true, it seems incumbent on us to ascertain what this form is, and to use it. But the fact seems to be, as shown by Bartholow, that even the very small doses, if given on an empty stomach, produce constitutional effects as readily as very large ones given with the food. It seems probable therefore, that most of the dose taken after meals is rendered insoluble, by the iron probably, and excreted in the feces, so that this method of dosage is uncertain and dangerous, as one never knows when conditions may arise in the gastrointestinal canal to render the whole dose absorbable, with toxic results. It is much safer and more effective to administer small doses before meals; and if a full physiologic effect rapidly produced is desired, to give a minute dose every hour until the eyelids begin to itch.

Murrell says that a child five years old will take nearly the adult dose; and that girls require larger doses of arsenic than boys. Bouchet and Lewald found arsenic in a nursing mother's milk.

Merck's Index gives the following data:

Arsenic bromide (tribromide). Dose 0.001—0.004 Gm.; maximum 0.01 Gm. Soluble in water.

Arsenic chloride (trichloride). Dose 0.001—0.004 Gm. Soluble in all proportions in alcohol; in ether and oils. Decomposed by water, with which it is incompatible.

Arsenic iodide (teriodide). Dose 0.001—0.004 Gm.; maximum single dose 0.008 Gm. Soluble in ether or carbon disulphide; seven parts water or thirty alcohol. Decomposed by water.

Arsenic sulphide (trisulphide). Soluble in alkalies, their sulphides or carbonates.

Arsenous acid. Dose 0.001—0.002 Gm.; maximum single dose 0.005 Gm., or 0.01 Gm. in a day. Soluble in water, very slightly in alcohol; freely in hydrochloric acid.

Copper arsenite. Dose 0.0005 Gm. every half-hour; maximum 0.006 Gm. Soluble in alkalies, slightly in water.

Potassium arsenate. Dose 0.003—0.006 Gm.; maximum single dose 0.006 Gm., or 0.02 Gm. daily. Soluble in water.

Sodium arsenate. Dose 0.001—0.008 Gm. Soluble in four parts water, two of glycerin, or sixty of boiling alcohol. This salt is less irritant to the stomach than most other arsenical preparations.

Iron arsenate. Dose 0.004—0.008 Gm. Soluble in dilute HCl.

Quinine arsenate. Dose 0.004—0.008 Gm. Soluble hot water.

Caffeine arsenate. Soluble in hot water.

Atropine arsenate. Contains 19.72 per cent arsenic and 80.28 of atropine. Soluble in water and alcohol.

Strychnine arsenate. Dose 0.001—0.004 Gm. Soluble in fourteen parts of cold or in five parts of hot water.

Antimony arsenate. Dose 0.0013 Gm.

Burggraeve ascribes a deobstruent value to antimony arsenate, in chronic pulmonary affections, and in muscular rheumatism.

The salient points on which to base the therapeutic use of arsenic are: first, its power of stopping glycogen formation; second, of checking emaciation; third, of causing gastric irritation when exhibited in toxic doses; fourth, of imparting immunity against plasmodial attacks to the red-blood corpuscles. It is not unreasonable to attribute to small doses a useful degree of irritation, with exaltation of function, corresponding to that produced by non-toxic doses of all other gastric irritants.

The arsenites are preferable to the less soluble arsenous acid for internal use, and their number, and the combination with such useful agents as strychnine, iron, quinine, caffeine, copper, etc., give an unusual opportunity for nice selection.

The observation of Ringer as to the curative power of arsenic in the peculiar affection of the tongue he described also favors the use of this agent in gastric affections, as the diseases of the tongue are so frequently dependent on disorders of the stomach.

Finally, we cannot too strongly urge the necessity of distinguishing between the effects of large and of small doses in administering arsenic. In malaria, where it acts directly as a germicide, the full quantity tolerated is obviously required; but in nearly all cases where arsenic has won favor it has been when given in doses far below the toxic point.

Caffeine arsenate is not a very stable salt. It has been employed in the migraines of chloroanemics, and for the hectic of tuberculosis.

Laura prefers iron arsenate especially in confirmed chlorosis and in anemias allied to a malarial influence. Burggraeve remarked that its use rapidly provoked a general stimulation, especially modifying the arterial circulation. In anemias with the herpetic diathesis, with functional disorders, and the local lesions dependent on it, iron arsenate does well.

Iron arsenate was given by Carmichael, Wernick and Biett, in cancer and lupus, in doses of 3 to 6 milligrams once or twice a day and applied locally as a 5-percent pommade. Burggraeve employed it in anemia, chloroanemia of delayed puberty, the purulent cachexia, the sanguine dyscrasias, scrofulosis, cancer, syphilis, etc. This salt being slightly and slowly soluble is best given in very small doses—gr. 1-67 every waking hour. The addition of nuclein increases its assimilation markedly.

Among those who look upon manganese as an essential constituent of the blood may be named Cantani, Clarus, Bourdach, Millon, Fourcroy, Burin du Buisson, Petrequin and Hannon; and the addition of this metal to iron follows as advisable. The indications are the same as with iron. It may be given with iron or alternately. Since potassium permanganate has proved of value in amenorrhea, when anemia coincides manganese arsenate should prove useful.

Laura, following Timmermans, employed quinine arsenate in chronic malarias, fevers with quick relapses, and paludal cachexias. In acute recent agues he evidently prefers the other quinine salts,

though quoting approvingly Bourrières and Bertoloni, who found the arsenate as prompt as inoffensive, curing with surprising rapidity; and Boudin and Morgant who claimed that against relapses arsenic possessed a power unknown and stranger to quinine sulphate. Many Italian clinicians, as Fenoglio, testified in like manner to the value of this salt in the dangerous malarias of that country.

In rebellious fevers, ataxic and adynamic, Burggraeve united the arsenates of quinine and strychnine, "an agent extremely precious in all the forms, really depressive in truth though not in appearance, of prolonged maladies, typhoid, typhic and infectious."

The arsenate of potassium, and still more that of soda, are distinguished by the rapidity with which they are absorbed and eliminated. Too little attention is given to the latter consideration, since it has been shown that arsenic may be retained in the body for months and cumulation seems more likely than with any other remedy. This points to the surpassing value of arsenic iodide, as the speediest of the arsenical salts in getting to work, and the safest in that it is the most rapidly eliminated. Besides, we have in it a double element of safety, in that both the components cause irritation of the conjunctiva and thus give warning of the beginning of toxic action. If, as Van Renterghem claims, arsenic acts principally by catalysis, we have this quality preëminently displayed by the iodide. Its principal application has been in maladies of the skin, when the stimulation of iodine has been indicated—dry, chronic forms, where the vitality is insufficient to inaugurate the curative processes. The writer has obtained such success from it in the treatment of arteriosclerosis, angina pectoris, and other maladies in which there was a deposit of morbid debris in the walls of the heart and blood-vessels, that he feels warranted in recommending this salt warmly. It is very active, and few adults will take more than four granules a day without soon developing evidences of overaction. The dose should be held just below this point, and continued for a long time—I have given it daily for eighteen months without harm.

Strychnine arsenate stands in a class by itself, being employed by Burggraeve as the vital incitant *par excellence.* Arsenic always tends to induce fatty degeneration. Given in the formative stages of acute maladies, we believe that it acts on the newly formed morbid deposits rather than on the normal histologic elements, and thus favors the rapid degeneration, deliquescence, absorption and elimination of these products of the disease. The rubbish is thus prevented from accumulating and is quickly cleared away. Hence, the

doses should be very small, to keep this action of the remedy within desirable limits. That this salt of arsenic became the favorite before this or any plausible hypothesis of its action had been framed, is no mean proof of its superiority.

So highly did Burggraeve value the arsenate of strychnine that he termed it affectionately his "warhorse," especially in suffocative catarrh, angina pectoris and all dyspneic maladies. Whenever it is necessary to reestablish the equilibrium between the nervous and myotic systems, this agent will accomplish the reunion and maintain it. It is applicable in all typhoid maladies, pyrexias, inflammations, nervous insufficiencies; and when associated with hyoscyamine, whenever spasm is a cause of the rupture of physiologic equilibrium, as in asthma, dysphagia, dyscrasias, physometra.

Faye especially urged the arsenates of quinine and strychnine in puerperal fevers, as well as in malarial, typhoid and zymotic forms in general and in typic neuralgias.

Van Renterghem succeeded with this combination in metrorrhagias; in acute cases giving one or two granules of each every half or one hour.

In leukemia and leukocythemia arsenic is more successful than iron. The arsenates, says Burggraeve, are to dyscrasias what the alkaloids are to pyrexias.

Since the introduction of the organic forms of arsenic, these have proved useful in several maladies, such as the sleeping sickness or trypanosomiasis, and syphilis. In the latter malady, surprisingly good effects have followed the use of cacodylic acid, atoxyl, arrhenal, hectine and salvarsan, all organic arsenics. In these the specific curative powers seem to be greater than those of the ordinary forms of arsenic, while the toxic property is much less. It is significant that these maladies, as well as malaria, in which arsenic has proved most effective, are all ascribed to protozoa. Besides, this remedy has been recently commended in maladies unquestionably infectious, but in which the specific cause is ultra-microscopic and passes through the closest filter.

The fact that arsenic favors the formation of lactic acid and the maintenance of hemic acidity may aid in explaining the preference for strychnine arsenate in the treatment of acute febrile maladies.

ARSENIC IODIDE

Standard Tablet—gr. 1-67; Gm. .001.

The iodide of arsenic has two important characteristics; both elements act notably upon the eyes, and the irritation denoting full

effect occurs more quickly than with any other preparation of either arsenic or iodine; and for this reason the remedial effect of arsenic is secured more promptly than with any other form of this metal.

Burggraeve utilized arsenic iodide principally in skin diseases, especially the dry forms where the pores of the skin are obstructed and crusts or furfuraceous scales formed.

Thirteen years ago the writer was consulted by a lady of advanced age who showed evidences of arteriosclerosis and was threatened with senile gangrene. She was given arsenic iodide, which was continued a year. The pain and other subjective symptoms subsided, the malady was apparently checked and to the present day has not made any progress, the senile arc then manifest being unchanged. Since that time this has been the writer's favorite remedy in this affection, and the results of its administration have been satisfactory to him and to his patients.

In treating those acute manifestations of syphilis, cerebral, ocular, nasal, etc., that are commonly met with maximal doses of potassium iodide, arsenic iodide has been substituted, with mercury biniodide and iodoform, from the belief that a quicker and more powerful effect is thus secured; and experience has justified this belief. The necessity for the quickest possible action is better comprehended if the physician realizes that while syphilis may be checked or cured, this does not restore life to dead tissues or continuity to ruptured nerve fibers. The superiority of the combination herein recommended over potassium iodide is manifest to the most superficial observer.

The dose of arsenic iodide is gr. 1-67 three or four times a day for an adult. Few persons can take more than five daily doses of this size without irritation of the eyes quickly following. The lady whose case is mentioned was thus affected by five granules a day; but took four a day for a year, with only benefit.

The iodides are exceedingly valuable preparations and it should be our study to find and our practice then to exhibit those which produce the greatest and most satisfactory results with the least irritation. These will be found in the newer preparations, arsenic iodide and calcium iodized.

ARSENIC SULPHIDE

Standard Granule—gr. 1-67; Gm. .001.

Orpiment, the yellow or trisulphide of arsenic, is not utilized in the materia medicas, but has won a place in the arsenal of alkalometry. We have employed it with great satisfaction for the ordinary

cases in which arsenic is given; as an alterative in skin affections, etc., etc. Its specific place, however, is as a remedy for microbic infections such as gonorrhea, especially for the socalled rheumatism, or septicemia. For this the writer introduced the treatment by calcium sulphide, gr. 1, and arsenic sulphide, gr. 1-67, four times a day, gradually rising to seven doses daily, or until the odor of rotten eggs on the breath and perspiration showed that the body was saturated with the sulphides. This effect is to be sustained for two weeks, or until the disease has disappeared.

Does arsenic sulphide here add anything to the effect of calcium sulphide? In several cases, when calcium sulphide alone did not appear as effective as was expected, the addition of arsenic sulphide was followed by immediate improvement.

Would arsenic sulphide alone do the work now accomplished by calcium sulphide? If so, the benefits are obvious; the smaller doses, ease of manipulation, permanency of product, etc.

This remedy gives remarkable results in acne and in many forms of skin disease. Gr. 1-67 after meals, with three to four Sulphur Comp. granules (formula credited to Dr. Buckley: Pulverized sulphur, gr. 1-134; extract nux vomica, gr. 1-67; podophyllin, neutral, gr. 1-67; collinsonin, gr. 1-134), will soon cause marked amelioration, especially if eliminative and antiautotoxic measures are taken at the same time. In ichthyosis it gives prompt results.

In albuminuria arsenic sulphide will be found of signal service. Doses should be increased to tolerance. In socalled "bronchial asthma" this remedy will prove efficacious if given in alternation with an acid. The cases most benefited are those in which there is profuse expectoration.

Eczema, provided it be of the dry and scaly variety, will respond to arsenic sulphide and saline elimination with regulation of diet, and if at the same time hepatic and renal action is kept up by the use of calomel and iridin, with subsequent saline draughts.

In prurigo, pruritus and psoriasis, mercury biniodide and arsenic sulphide may be given alternately by weeks with good results.

Arsenic sulphide is one of our best cellular alteratives where surface tissues and other excretory structures are involved. It must be known to be appreciated and must be used right and associated right to produce the results outlined.

Its use might be extended to the whole range of maladies due to plasmodial parasites, malaria, trypanosomiasis and syphilis, as well as to those that are probably plasmodial, such as yellow fever and dengue.

ASCLEPIDIN

Standard Granule—gr. 1-12, Gm. .005.

Asclepidin is a concentration from the root of Asclepias tuberosa.

The virtues depend on a glucoside obtained by Quackenbush in a crystalline form. It has not been produced commercially.

King says asclepias is diaphoretic, diuretic, laxative, tonic, carminative, expectorant and probably antispasmodic. Being non-stimulating it may be used as a diaphoretic in the highest fevers. The secretion from the skin produced by it closely resembles the normal insensible perspiration. The solids excreted are largely increased, rather than the fluid. Even when there is free perspiration asclepias may be needed to increase the solids excreted. It does best when the fever is not too high, the skin is slightly moist, the pulse vibratile and not too rapid. Aconitine should be added if the pulse be rapid, weak and small; veratrine if strong and bounding.

Therapeutics.—Asclepidin increases the respiratory secretions and favors expectoration. Its power of naturally stimulating the skin renders it efficient in colliquative sweating. It has been termed pleurisy root from its value in this malady, where it may be combined with bryonin or aconitine. In pleurodynia, intercostal neuralgia and rheumatism, and in pericardial pains it is effective. Its chief action being to relax arterial tension, it is best suited to acute attacks. It is a useful adjuvant in early pneumonias and pleuropneumonias, pulmonary hyperemias and extensive bronchitis, in the early and the convalescing stages.

It relieves dry coughs if given following lobelin. It is among the best remedies for catarrhs of children. In phthisis it relieves the cough and the mucous irritability. It is one of the best remedies for colds, and for all respiratory and gastrointestinal catarrhs when due to recent colds. Asclepidin is of benefit in the gastric troubles of children, catarrhal diarrheas and dysenteries, the headaches of indigestion, flatulent colics, dry skin diseases, neuralgias and rheumatism with free sweating. It favors the eruption in the exanthemata, and sometimes relieves painful inflammations by the perspiration it induces.

Scudder gives these specific indications for asclepias: Pulse strong, vibratile; skin moist; pain acute, seemingly dependent on motion. King says the skin may be hot and dry or inclined to moisture, urine scanty, face flushed, vascular excitement marked in parts supplied by bronchial arterioles, in serous inflammations, and gastrointestinal catarrhs caused by recent colds.

Ellingwood says asclepias is specific for pleuritic pains, facilitating the rapid removal of the effusion. For stomach pains it should be given in full and continued doses. It soothes the entire intestinal mucosa.

For acute maladies asclepidin may be given in doses of gr. 1-12 to 1-4 in a cup of hot water, repeated every half-hour till effect. In chronic maladies the dose is a grain before meals and at bedtime.

ASPARAGIN

Standard Granule—gr. 1-67, Gm. .001.

Asparagin occurs in the potato, the leaves of belladonna and the root of the greater comfrey. Huesemann found in the root of the marshmallow two percent, and Robiquet detected it in licorice root. The seeds of the vetch contain it in large quantities during their germination, and it is present in the plant during flowering.

Asparagin occurs in transparent rhomboidal crystals, colorless, very hard, of a cool, nauseating flavor. It is soluble in forty parts of cold water, four parts of hot water, insoluble in alcohol. The extractive matter of asparagus sedates the heart and induces diuresis (Dendrick); but Falck denies this.

Asparagin is a glucoside found in many plants, but in greatest quantity in the vegetable asparagus. The well-known odor imparted to the urine by eating asparagus is not due to this principle, however, but to methyl mercaptan. To this odor is possibly due the repute which asparagin holds as a diuretic; a doubtful matter, as neither Falck, Jacobi nor Posner obtained any diuresis from doses up to fifteen grains. Nor was the pulse notably affected. Huesemann also failed to obtain any useful effect from it in dropsies dependent on heart disease.

But there are other functions of the human body besides the few that have been selected as tests of remedies. In the plant world asparagin fills a place analogous to that of urea and uric acid in the animal, as one of the principal products of albuminoid decomposition. But while urea and uric acid become useless to the animal and must be eliminated from the body, asparagin, produced by the destruction of a molecule of albumin, can be immediately utilized in the green plant, and serves to build a new molecule of albumin. In the legumes asparagin, formed and accumulated at the moment of germination and produced by the destruction of the reserve of albuminoids utilized during germination, disappears subsequently when the young plants become charged with chlorophyll. Thus the

disappearance of asparagin coincides with the formation of an equivalent quantity of a new albumin.

Therapeutics.—It is likely that asparagin increases the excretion of solid matters by the kidneys, since it has won some repute as a remedy for gout, its effects being milder than those of colchicine. As long as all diuretics are judged by their power of reducing dropsical effusions, there is little chance of estimating the true value of such remedies.

Asparagus has been accredited with aphrodisiac and emmenagog properties. It sometimes causes a urethral discharge like that of gonorrhea, and its use may increase the irritation of that malady. It has been used in place of ergot to stimulate uterine contractions after miscarriage or in the later stages of labor. Sometimes it causes serious disturbance of the renal function. Its use has been proposed as a means of testing the permeability of the kidneys. If the characteristic odor of asparagus in the urine does not follow the eating of this vegetable, then any remedy normally excreted by the kidneys, when given to this patient, is liable to be retained in the body and cause poisoning.

Laura asserts that asparagin possesses the diuretic properties of the plant. He found it especially useful when the abnormal congestive state, of the renal apparatus, irritative or phlogistic, rendered the employment of irritant diuretics improper, but in which diuresis appeared to be indicated. In these also the compound official preparations were unacceptable or badly borne by the enfeebled stomach, as in dyspeptics, and patients who refuse to take voluminous doses. "The granule respects the function of the stomach, rarely intact in these cases, and this is a matter of moment for all patients." He advises a dosage of five to ten milligrams, repeated as often as necessary to induce diuresis. The remedy being harmless the doses may be increased, and the drug continued indefinitely, since it does not fatigue the stomach or trouble the organic equilibrium of the kidneys, so easily and so perilously disturbed by irritant diuretics. We can not take too much care to preserve the anatomic integrity of the renal filter, for if this organ is injured more or less gravely, it almost surely entrains, besides maladies grave and very painful, the ruin of the entire organism.

One of the perilous emergencies we meet is in the treatment of acute nephritis, for instance, as it follows scarlatina. It is absolutely essential to the continuance of life that the urinary passages be swept free of the debris that blocks the uriniferous tubules, but any but the smallest doses of such stimulants as the diuretic volatile oils are

apt to cause such congestion as to result in total suppression of the urine. Asparagin would seem well suited to such cases, and might receive a trial. It should also be tested as to its effect on the excretion of urinary solids. Clinically we have found decided improvement follow its administration in cases where the excretion was far below the normal, but our experiments were too few to decide the question. Deficiency in the excretion of urea may be sometimes due to an inability to utilize in its formation such material as is presented, and asparagin may meet this need. We repeat—this glucoside deserves further trials. Too many good clinical observers have reported satisfactory results from its use for us to be contented with the meager and contradictory information gleaned from the literature.

There is something in asparagin—what is it?

Dr. E. A. Welch, of Sutton, Mass., reported two cases of cystitis in which he found benefit from asparagin. Several others have reported this agent as giving a more pronounced diuretic action than the foregoing account would indicate.

Van Renterghem suggests granules of a centigram each, of which five may be given every quarter-hour in acute cases; in chronic maladies this dose may be employed four times a day. He thinks it might be useful as a succedaneum to digitalin or to colchicine, or as an adjuvant to be administered with these medicaments.

The truth is that both the physiologic action and the therapeutic application of asparagin remain to be determined. That it is accorded a place here is due to our conviction that it deserves such study as is suggested.

ASPIDOSPERMINE

Standard Granule—gr. 1-67, Gm. .001.

Some years ago the medical profession welcomed a new applicant for favor, in the form of quebracho, an extract from the bark of an evergreen tree of South America. It was presented as a specific remedy for the symptom of dyspnea, occurring in the course of any malady. Investigation showed that this extract contains at least six alkaloids, whose properties differ to some extent, though, as in the case of the digitalis glucosides, there is a strong similarity in their action.

Harnack and Hoffman found that aspidospermatine causes in the frog paralysis of respiration and of all striated muscle, in-

cluding the heart. In mammals the most marked action is on the respiration.

Quebrachine exerts a precisely similar action on the frog, but is twenty times stronger in mammals, causing death by respiratory paralysis.

Quebrachamine closely resembles aspidospermine.

Aspidosamine closely resembles aspidospermatine on the respiration and muscle fiber, but also paralyses the motor nerve-ends.

Wood says that quebrachamine in small doses causes a slight elevation of blood pressure without much change of respiration. After large doses there is a marked rise in blood pressure and quicker breathing, but also cerebral convulsions. Aspidosamine stimulates respiration some, but depresses the circulation much more. Aspidospermine in moderate doses increases breathing somewhat without seriously affecting the circulation, but overdoses depress respiration and cause convulsions.

Quebrachine enormously increases the depth and rate of respiration. The effects on the circulation while at times marked were subordinate and variable. "The increase in respiratory activity caused by quebrachine I have never seen paralleled by any other drug, either in degree or duration. After moderate doses of morphine, chloral or ether, quebrachine distinctly increased the breathing, but when the depressant dose had been large enough to cause dangerous depression of function the addition of quebrachine was followed by an immediate cessation of respiration." After small doses the pulmonary tissue was pale. Whenever respiration was greatly increased there were found sharply localized areas of intense congestion scattered through an anemic lung. Many seemed to the eye hemorrhagic. These effects Wood attributes to a specific local influence, not an ordinary chemical irritation.

This emphasizes our suggestion to use only small doses.

Aspidospermine was discovered by Hesse. It is soluble in alcohol, in 106 parts of absolute or 48 parts of 90 percent ether, 6000 of water, and easily in benzoin or chloroform. The salts are very soluble. It is very bitter. It forms colorless, hard prisms, or fine acicular crystals. Potassium iodide, Mayer's reagent, potassium-bismuth iodide, bromine, and phosphomolybdenic acid, give white precipitates with very dilute solutions; picric acid with a solution 1-1000; but tannic acid only in concentrated solution. Concentrated sulphuric acid and Frœhde's reagent dissolve aspidospermine without coloring. In diluted perchloric acid it dissolves on heating, with red color.

Physiologic Action.—Small doses by stimulating the center make the breathing more rapid and deeper, slow the heart and lower the temperature. Large doses cause tonic contractions and convulsions. Lethal doses render respiration slow, weak and arrhythmic, death being due to apnea. The heart continues to contract after the breathing ceases. The effect is especially on the medullary centers, as shown by nausea and the respiratory changes; and on the spinal cord, as indicated by the convulsions, and increased reflex excitability. The muscular fibers are weakened and finally paralyzed in the frog, but not in mammals. The circulation is weakened by the nausea, and directly by lethal doses (Cushny). Eloy and Huchard noticed diarrhea and diuresis occurring sometimes, and a diminution of the hemoglobin. The venous blood of animals after toxic doses is red, like that of animals killed by bulbar puncture. Penzoldt explained this by attributing to aspidospermine the power of increasing in the red blood cells the capacity of absorbing oxygen, and depriving them of the power of parting with it to the tissues.

While this alkaloid causes nausea in overdoses it does not occasion vomiting, even in excessive doses. It increases the mucous secretion of all the respiratory tract, and also the saliva.

Quebrachine has the formula $C_{21}H_{26}N_2O_3$. It forms delicate acicular crystals, intensely bitter in solutions, almost wholly insoluble in cold water or alcohol, alkalies or ether, and easily soluble in chloroform and in boiling alcohol. It is dextrogyrate. It gives no color with iron chloride. Boiled in perchloric acid it becomes yellow. A solution in concentrated sulphuric acid becomes bluish in a few minutes; on adding potassium bichromate it becomes blue, and finally reddish brown.

Quebrachine is a powerful respiratory paralyzer; Gram 0.005 (gr. 1-12) injected intravenously kills a rabbit instantly by respiratory paralysis. In mammals the paralysis is preceded by a brief period of increased irritability, the rate and depth of respiration being increased, and muscular spasms following. In frogs it paralyzes the motor apparatus, first affecting the peripheral respiratory nerves, whereas the other quebracho alkaloids affect the centers (Liebreich). The pulse is slowed to stopping, but only after respiration ceases. In toxic doses the breathing deepens, the rate of respiration being unaltered; the quantity of air inhaled is greater, but the excretion of carbonic acid gas does not correspond. The blood absorbs and retains more oxygen (Penzoldt), the medulla lacks oxygen, and dyspnea results.

Quebrachine also lowers the temperature, even small doses causing a fall of 1.2 to 1.4 degrees F. in ten minutes (Eloy and Huchard); at the same time the secretion of urine is increased.

Schiffer found that an extract of quebracho bark caused in a mammal (rabbit) muscular weakness, followed by paralysis, with greatly diminished reflex excitability, the deepest narcosis, rapid breathing, the heart and pupils being unaffected. Death was preceded by convulsions. The motor nerve-trunks even before death were almost devoid of functional activity.

Eloy and Huchard found that after removing quebrachine, hypoquebrachine, aspidospermine and aspidospermatine, the residuum had some effect on the sensibility, although the four bodies removed had none, but produced tonic convulsions and reduced the temperature. Aspidospermine greatly excelled the other alkaloids in its effect on respiration.

We see therefore that the physician who prescribes the extract of quebracho has at his command an agent of undoubted power. It may, if aspidospermatine be predominant, cause respiratory sedation and muscular debility to a certain extent; if quebrachine be the predominant alkaloid he will get twenty times more of the same effect. If aspidosamine be the principal alkaloid in the sample he secures, he will have in addition to cope with paralysis of the peripheral termini of the motor nerves. Should he be fortunate enough to secure a preparation in which all the foregoing exist in small amount, but aspidospermine is richly present, he will obtain the respiratory stimulation he seeks, with lowered temperature and slower pulse, without any weakening of the heart. He may find the reflex excitability lowered or heightened, as the case may be. Possibly the bowels will be loosened or the urine increased in quantity, but then again nothing of the sort may occur. Maybe it will induce profound narcosis, or drop the temperature one to four degrees, or affect the sensory nerves. In short, there is a terrifying uncertainty as to what effects are going to follow the administration of quebracho, that is calculated to keep the physician guessing. Probably his best plan after prescribing it is to sit on the fence until summoned, with stomach-pump in hand.

The effects of aspidospermine are distinct, uniform and unvarying; their quality and degree of action can be calculated to a nicety—the effect is certain when the indication is presented.

Therapeutics.—Aspidospermine has been employed for the relief of dyspnea, as occurring in the course of asthma, emphysema and other respiratory maladies. It is less effective in the dyspnea of

pulmonary tuberculosis. Harnack asserts, however, that the best quebracho alkaloid for this purpose is quebrachine.

Eloy and Huchard recommend aspidospermine as an antipyretic in fevers. Froude gave it in typhoid fever to lower the temperature and stimulate the lungs. It has proved of service in every form of dyspnea, bronchial, cardiac, nervous, even in that of uremic origin (Wood), as well as in emphysema and in spasmodic croup.

Picot states that taken before hill-climbing, it increases the respiratory endurance.

Its effect in relieving cyanosis is marked (Shoemaker). In a child with double pneumonia, it decidedly improved the breathing and the heart-action (Lawrence).

In acute rheumatism and in serous inflammations, it sedates the pulse and lowers the fever (Shoemaker).

Dosage.—The dose is somewhat doubtful, and Penzoldt says that it must be separately ascertained for every case. As Gram 0.003 (gr. 1-22), hypodermically, causes muscular tremor, it is best to begin with doses of Gram 0.0005 (gr. 1-134), repeated every hour or oftener till the desired effect has been obtained. The dose thus ascertained may be given subsequently at once.

For hypodermic use the chloride is suited by its ready solubility in water. Dose Gram 0.0005 (gr. 1-134), not exceeding Gram 0.002 (gr. 1-33).

Or for hypodermic use dissolve Gram 0.2 of aspidospermine in water 10.0 C. c. with the aid of a trace of sulphuric acid, neutralizing if necessary with sodium bicarbonate (Bocquillon-Limousin). The doses given for the commercial aspidospermine cannot be taken as applying to the pure product now employed under that name.

Quebrachine hydrochlorate dissolves easily in hot water and remains in solution on cooling. The average dose is Gram 0.005—0.1 (gr. 1-12—1 1-2) three times daily; or better, Gram 0.001 (gr. 1-67) every hour or oftener until the desired effect is obtained. It is of use in asthma, emphysema, bronchitis with marked nervous irritability and dyspnea, and may be used in affections characterized by hyperpyrexia.

If the physician is not going to delve deeply into the active principles of quebracho he would best content himself with two things, and should so fix them in his mind that they will stick forever. (1) Never use the extract under any circumstances if the alkaloids are obtainable. (2) Always use aspidospermine to the exclusion of the others and learn how to use it right, remembering

that it relaxes spasm, stimulates the breathing mechanism and slows and steadies the heart, effects desired in all cases of dyspnea; therefore the indication. Give aspidospermine in dyspnea; give it right and you will not be disappointed.

ATROPINE

Standard Granules—Atropine sulphate, gr. 1-500, Gm. .000125; atropine sulphate, gr. 1-250, Gm. .00025; atropine valerianate, gr. 1-250, Gm. .00025.

Of all the remarkable agents in the wonderful alkalometric armamentarium, none is of greater interest than atropine. The more the science of drug-action is studied the greater is the tendency to lift this powerful alkaloid into the place heretofore occupied by morphine, a monarch who has forfeited his crown by bad behavior.

The group of plants containing atropine has been recognized from the earliest days of the medical art as possessed of powerful influences for good or evil over the human body. As poisons the names of deadly night-shade, henbane and death-apple represent the popular idea of belladonna, hyoscyamus and stramonium.

In medical practice they were recommended for about everything in the list, especially for maladies not readily controlled by ordinary agents; but the general repute of the whole group was—unquestioned power but uncertainty of action, and therefore unreliability. They were remedies "to be tried," and that this uncertainty should exist in the case of these ancient remedies, after thousands of years' use, shows well the true status of the science of therapeutics in this, the twentieth century of Christianity; though in truth the use of these drugs antedated the present era by at least twenty centuries more.

We now know that the cause of this uncertainty lay in the varying chemical composition of the plants. Nature is unvarying and in her is no shadow of uncertainty; and the same conditions of sunshine, heat and moisture accomplish the same results, with of course the other influences of soil, competition, etc. And as these conditions vary she produces varying proportions of atropine in each of these plants, and varying proportions of certain other alkaloids as well. She leaves to the enlightened reason of man the task of separating these principles and utilizing their properties.

Belladonna contains atropine with hyoscine, hyoscyamine, atropamine, and belladonnine. Atropine predominates.

Hyoscyamus contains hyoscyamine and hyoscine, with a little atropine. Either may predominate.

Stramonium contains atropine, hyoscyamine and hyoscine.

Duboisia myoporoides contains hyoscine or hyoscyamine and other alkaloids. Another duboisia contains piturine, closely allied to nicotine.

Scopolia contains hyoscyamine, hyoscine and a little atropine.

Mandragora probably contains a mixture of these alkaloids.

The leaves of tobacco and potato contain some of these alkaloids. Decomposing fish and meat contain a ptomaine, ptomatropine, whose effects closely resemble those of atropine.

Not one of these sources supplies any one of these alkaloids without the other, or in unvarying proportions. Belladonna comes nearest to giving a uniform effect, the atropine nearly always predominating.

These agents affect man and the dog easily, while other animals feed upon the plants containing them with impunity.

Atropine was isolated in 1833 by Geiger and Hesse, but Mein had already discovered it in 1831. It crystallizes in prismatic needles. It is soluble in 300 parts of cold water or in 58 parts boiling water; is very soluble in alcohol, and this solution is precipitated by a very little water. It is soluble in 35 parts of cold ether, six of boiling ether, three parts of chloroform and very easily in amylic alcohol. The salts crystallize with difficulty, and are readily soluble in water or alcohol, but very slightly in ether.

Sollmann thus arranges the mydriatic alkaloids: Atropine and hyoscyamine are isomeric tropein alkaloids, tropeic acid-tropins, the former being optically inactive while hyoscyamine is levogyrous. Atropine has recently been found to be a mixture of two forms of hyoscyamine. Atroscine and scopolamine are isomeric tropeic acid oscins, of which the former is like atropine optically inactive, scopolamine also levogyrous. A mixture of these two forms the *commercial* hyoscine. Belladonnine and atropamine are isomeric belladonnic acid tropeins, differing from atropine by the absence of a molecule of H_2O. Homatropine, a synthetic, is oxytoluic acid-tropin; benzoyltropein is benzoic acid-tropin. Ptomatropine is an as yet unisolated alkaloid or ptomaine of decomposing meat, which induces symptoms similar to those of atropine. Hyoscyamine is more plentiful in the young plant, and may be the original alkaloid from which atropine is derived, this being more abundant in older plants. He sums the action of the group as comprising first excitation and then paralysis of certain parts of the central nervous system, particularly the cerebral and medullary centers, primary paralysis of the peripheral ends of the nerves of secretion, the pupil

contractors and the accommodation, and those of unstriped muscular fiber, especially the intestinal and the cardiac (here exactly antagonized by muscarine); slight stimulation and then paralysis of smooth and cardiac muscle and other cells; paralysis of sensory nerve ends on local application thereto. "The quickened pulse is the principal effect of moderate doses of atropine on the circulation. The blood pressure is scarcely altered, but there may be a slight rise, from stimulation of the vasomotor center. This stimulation is always slight, and may be entirely absent; it is replaced by vasomotor depression rather early. Large doses depress the vasomotor center profoundly, so that the pressure falls very low." This disposes of Wood's objection to atropine as a hemostatic, in that as he claimed it increased vascular tension. The flushing of the skin Sollmann attributes to vasodilator stimulation, and not to vasocontractor paralysis; and in this we fully agree, as the phenomena are evidently active and not passive.

Atropine is eliminated by the kidneys, and this is practically complete in thirty hours. Some is broken up in the body. The flesh of animals that tolerate atropine becomes so impregnated with it as to be toxic if eaten by man.

Tcherkesson draws attention to the utility of atropine injections in strangulated hernia. He uses two milligrams at a dose. Half an hour after the injection has been given an attempt at gentle taxis is made. The patient is put in the genupectoral position. A second injection is given if there is further difficulty. The author strongly urges that every strangulated hernia should be operated upon, even in cases where this method has been successful. Otis says that Hare is mistaken in assuming that there is an increase of blood pressure in all cases of hemorrhage. His observations show that when there is a low blood-pressure ergot is of value, and only does harm in other cases. His observations would have been much more important had he used but one remedy in each case, but when one gives morphine, atropine, nitrates and ergot, possibly heroin, in the same case, it is impossible to say to what the benefit was due. It is significant, however, that in the seven cases in which he gave atropine, the hemorrhage ceased promptly in all. He praises aconite, especially in those cases in which the blood tension was high.

Woltke states that, in two reported cases, nothing controlled hemoptysis until atropine was injected subcutaneously; the doses being from 2 to 6 milligrams, repeated on six consecutive days. One patient had been ineffectually treated with innumerable

measures, including ergotin, hydrastis, morphine, iron and turpentine; the rebellious hemorrhages from the lungs threatening speedy dissolution.

Physiologic Action.—Van Renterghem gives the following symptoms, as they appear successively after taking atropine: Dryness of mouth and throat, thirst, disordered vision, paralysis of accommodation, alteration of the voice, aphonia, sense of cold followed by rapid pulse, redness of the face, vertigo, headache, and delirium. If the alkaloid is then discontinued, the symptoms subside in reverse order in twelve hours, except those pertaining to the eye, which may last longer. Very large doses cause the same symptoms but more accentuated, the stage of excitement is short and quickly followed by that of paralysis; deglutition is impossible; dysphagia, rabic symptoms, injected conjunctivæ, eyes prominent, face crimson, iris disappeared, furious delirium, ending in complete adynamia, fall of pulse, which had reached 150, lessened heat, respiration difficult, cutaneous anesthesia, paresis, soporous state, convulsions general and partial, retention and then incontinence of urine and feces, weakening and irregularity of the pulse, and death by asphyxia in three to thirty-six hours.

The muscular motor nerve-ends are paralyzed by large doses; as well as the cutaneous sensory nerve-ends, hypodermic injections producing more local anesthesia than morphine. Gubler mentions a case where the patient after a full dose was unable to button his clothes, the tactile sense being abolished and the muscles having lost their power.

While small doses paralyze the intracardiac vagus ends, permitting an enormous rise of the pulse-rate, it is evident that other portions of the heart are influenced by atropine, since it lifts the paralysis caused by chloroform, potash salts, oxalates, cholates, apomorphine, copper, zinc, antimony or quinine (Luchsinger).

Atropine stops the secretory action of glands by a direct influence over the nerve ends, the vasomotor influence going for nothing.

It arrests the peristaltic movements of the intestine completely when they depend only on the motor nerve-centers (Schmiedeberg). The paralyzant action is best shown when the circular fibers are in spasmodic contraction. This action is exerted on the stomach, spleen, bladder, uterus, bronchi, etc.

Small doses lessen the excitability of the ganglionic system of the intestine, bladder, ureters, uterus, perhaps paralyzing the smooth muscular fibers themselves (Bezold and Bloebaum).

The scarlatiniform redness of the face and upper part of the body may depend on the local vasodilation, or rather on the rapid pulse and rise of blood-pressure (Van Renterghem).

The influence of atropine on the vasomotor nerves explains its antiphlogistic effect. Zeller observed that a solution of atropine sulphate in a neutral solution of sodium chloride dilated the arteries, accelerating the circulation in veins and capillaries not dilated. The passage of white globules into the tissues was checked, the amœboid movement of emigrated cells was lost on contact with atropine, and they became round and opaque.

Atropine exerts its effects markedly on the peripheral nerve-ends, paralyzing the pupil contractors and accommodation apparatus of the eye, the cardiac inhibitory centers connected with the vagus, the intestinal and other unstriped muscular fiber, and the secretory nerves of many glands. Large doses affect the cerebrum, causing delirium.

The conjunctiva is most sensitive to atropine, which diffuses itself into the ocular tissues without entering the blood, as one pupil, or even a part of one pupil, may be fully dilated without affecting the other pupil or the rest of that one. The drug affects the ends of the oculomotor fibers in the muscle-cells of the sphincter. If thoroughly atropinized no direct irritation of the oculomotor in the cranium will affect the pupil; though if the patient be insulated and a static current applied to any part of the body the iris will contract (Neiswanger). In birds the iris consists of striated muscle fiber, and this is not affected by atropine. To paralyze the accommodation requires larger doses and longer time.

Atropine lessens the number of the leucocytes, and the excretion of uric acid (Horbaczewski).

When atropine is given internally, in doses of Gram 0.001 (gr. 1-67) thrice daily, it affects the eye, the glandular innervation and the motion of organs containing unstriped muscle-fiber, including the heart. In moderate doses atropine abolishes the action of the chorda tympani on the salivary secretion, but not the influence of this nerve over the dilation of blood-vessels, nor the function of the gland-cells. For irritation of the sympathetic has the same effect after the atropine intoxication as before it, the gland-cells secreting thick and scanty saliva (Heidenhain). Physostigmine in large doses, injected into the artery of the gland or its parenchyma, overcomes this paralysis, unless the dose of atropine is overwhelming, and active in the general circulation. All the salivary glands are affected alike by atropine. Minute doses stop the secretion of the

mucous glands of the tongue, controlled by the glossopharyngeal. The impairment of the sense of smell is due to drying up the nasal mucous secretion.

On the glands of the digestive apparatus atropine acts less energetically. The secretion of pepsin and hydrochloric acid is checked by it. The pancreatic secretion is checked, and simultaneously the passage of substances from the stomach into the duodenum is completely prevented (Pawlow). Irritation of the vagus excites pancreatic secretion, which is limited but not entirely stopped by atropine (Pawlow). The increase of pancreatic secretion by muscarine is completely suppressed by atropine, but the stimulation of bile-secretion by muscarine is only lessened by atropine. This would indicate the value of atropine as a remedy for hyperchlorhydria.

The amount of urine and of urea excreted is lessened by intravenous doses of atropine, Gram 0.0015—0.002 (gr. 1-43—1-33) per kilo of body-weight. This decrease is prevented by the free ingestion of water, salt and urea. Small remedial doses increase urine excretion.

On the perspiration the effect of atropine is strictly analogous to that on the sweat-glands. Reflex and direct irritation of the secretory nerves are alike useless, even after small doses of atropine (Luchsinger). Pilocarpine or physostigmine applied locally restores the secretion and the irritability of the centrifugal secretory nerves.

It is less certain that atropine directly lessens the secretion of milk and of the respiratory mucosa. The action of this agent on the blood-vessels may account for the clinical observations made in this respect, which certainly show a decrease in these secretions.

The nerve-ends in unstriped muscle-fiber are paralyzed by atropine, as those of striated fiber are by carmine. When under the toxic influence of atropine, irritation of the vagus will not produce gastric or intestinal motion. Small doses of atropine stop peristalsis, while large doses directly irritate the intestinal musculature, and even with small doses the previously quiet intestine will begin peristalsis (Liebreich). But exceedingly small doses by paralyzing inhibition facilitate the movement of the bowels (Brunton).

The paralysant dose of atropine varies with different organs. The bladder retains irritability when the esophagus is paralyzed.

Atropine acts on the circular muscle-fibers of the arteries locally and from the vasomotor centers. Added to the blood supplied an exsected living organ, the current is slowed briefly and

then much accelerated, showing the relaxation of the circular arterial muscles. By exciting the vasomotor center the vascular tension is raised. Sollmann states that the increase of vascular tension caused by atropine is slight, is only noticeable after small doses and not always then. It is speedily followed by very decided vasodilation, from vascular relaxation. In dogs, after large doses, Gram .001 per kilo, the cutaneous vessels dilated while the cerebral vessels contracted, and the arterial tension was raised (Albertini). This central effect is transmitted mainly by the cervical sympathetic, and when this is severed neither dilation nor contraction occurs.

On the heart even small doses paralyze inhibition, the pulse-rate in man increasing. No amount of irritation of the vagus will slow the pulse or stop the heart under atropine. So also dyspnea and irritability lose their effect on the heart. For some unknown reason the heart first slows when a toxic dose—Gram 0.005 (gr. 1-12)—of atropine is taken. Yet the slow pulse of muscarine, which stops the heart in diastole, is promptly quickened by atropine; while muscarine is unable, in any dose, to antidote the effects of atropine. Large doses of the latter directly paralyze the muscular fibers of the heart.

On the respiration atropine acts by paralyzing the vagus ends, and slowing the breathing. But by its action on the respiratory center in small doses it prolongs and deepens the respirations.

On the brain atropine acts as an irritant, in large doses causing excitement, unrest, insomnia, haste in movements and combativeness. In full intoxicant doses it causes hallucinations of sight and hearing, delirium mostly cheerful, erotism, impulse to constant activity, eventuating in convulsions; followed by paretic symptoms, syncope, anesthesia, and sopor. Very large doses finally paralyze striated muscle, like curarine.

Some tolerance of atropine may be acquired, but cumulative effects may occur ending in death.

Atropine often causes a rise in temperature, independent of the convulsions and circulatory changes. The heat radiation is increased but the heat-formation still more. This is due to a direct action on the cerebral heat-center (Ott).

Synergists.—The mydriatic group, belladonnine, homatropine, duboisine, daturine, hyoscyamine, mandragorine, are probably all forms or compounds of atropine. Among auxiliaries are hydrocyanic acid, as mydriatic, analgesic and cough sedative; quinine as an antiphlogistic; cicutine as a paralyzant of motor nerve-ends, analgesic and mydriatic; morphine, although it con-

tracts the pupil and congests the brain, suspends bronchial and intestinal secretion and calms pain; strychnine raises the general tonicity and augments the debilitated contractility of the longitudinal muscular fibers in cases of mixed paresis and spasm, often present in asthma, dysuria, retention of feces; camphor monobromide, gelseminine and cypripedin as antispasmodic and sexual sedatives; quinine and ergotin in combating hyperemia and as oxytocics; camphor, capsicum and glonoin in forcing out retarded eruptions.

Antagonists.—Nicotine is held by some to be a synergist, but seems rather an antagonist, as it contracts the pupil, and augments all the secretions, especially the sweat and saliva.

Muscarine excites the parts of the peripheral organs paralyzed by atropine, slows the pulse, lowers arterial pressure, increases saliva, tears, sweat, mucous secretions, bile, pancreatic juice, causes contraction of the pupil and spasm of accommodation, tetanic contraction of stomach and intestines, of bladder, spleen and uterus.

Pilocarpine and nicotine possess properties analogous to those of muscarine. The excitation of the peripheric terminations of the inhibitory nerve of the heart produced by these alkaloids is soon followed by paralysis, as the primitive myosis is succeeded by a light mydriasis. Both augment glandular secretion and excite contractions of the stomach and intestines. Atropine prevents or sedates these symptoms.

By its special action on the secretion of the bronchial mucous glands apomorphine is the antipode of atropine. But nevertheless we can serve ourselves with both at once, the apomorphine to diminish the viscosity of the bronchial mucus, the atropine to relax spasm.

Physostigmine, which excites the muscular system of the life of relation as well as that of nutrition, and tends to paralyze the whole central nervous system, is but illusory as an antagonist. Experimenting on a cat, by giving successively muscarine, atropine and physostigmine, we can cause spasm of the intestine, then complete detention, and again spasm; myosis and accommodation spasm, then pupil-dilatation and accommodation-paralysis, finally again pupillary contraction; the salivation caused by muscarine is arrested by atropine and restored by physostigmine. Probably physostigmine excites the muscular fiber and gland tissue thereby masking or neutralizing the paralysis of the peripheric nerve-ends produced by atropine.

Gelseminine, cicutine and the bromides combat the cerebral hyperemia of atropine. Aconitine does so also.

An exact antagonism of medicinal agents is unknown. One usually modifies the apparent effect of another by acting on some other part of the bodily mechanism.

Atropine is an effective remedy in poisoning from the fly fungus, Amanita muscaria, or its alkaloid muscarine (Schmiedeberg). In nicotine poisoning the stage of irritation is combated by atropine, but the sudden reversion to paralysis nearly related to that of atropine, suggests caution (Kobert). More important is its antagonism to morphine. The lowering of vascular tension and slowing of respiration caused by morphine are directly antagonized by atropine. Failure may be ascribed to overdosing with atropine, its paralytic effects becoming manifest. But morphine is far from being a counter-poison to atropine.

Children bear atropine much better than adults. Flaxen blonds are extraordinarily liable to its action, even in the smallest doses. Inebriates are apt to become wildly delirious from ordinary medicinal doses, of Gram 0.0005 (gr. 1-134). Idiosyncrasies are common. This remedy should therefore be given in very small doses, repeated quickly till the desired effect is manifest.

Therapeutics.—As a mydriatic atropine has become indispensable to the oculist, from the uniformity, certainty and power of its effects. A solution of Gram 0.06 (gr. j) to Gram 8.0 (two drams) of distilled water is usually prescribed, five drops being applied to the lower conjunctival fold every four hours for two days. This dilates the pupil fully and paralyzes the accommodation.

Homatropine may be preferable as a pupil dilator but cannot replace atropine in the treatment of ocular maladies. A single application may determine the access of glaucoma, hence the intraocular tension should always be tested before applying atropine. In superficial inflammations of the cornea with photophobia, especially if complicated with maladies of the iris, atropine acts by arresting the amœboid movement and migration of the white cells, and by preventing, by arterial dilatation and acceleration of the blood-current in the inflamed part, the adhesion of wandering cells to the lining of the capillaries and veins (Binz).

Deep corneal ulcerations threatening perforation, and conditions with increased intraocular pressure, contraindicate the use of atropine. Affections of the iris, however, form the special field for atropine, its instillation being prophylactic. Adhesions due to inflammation can often be prevented, synechiæ ruptured by atro-

pine, alone or alternated with physostigmine. Van Renterghem speaks of the improved results secured from the use of atropine when conjoined with the internal use of aconitine, veratrine and digitalin for fever and inflammation, quinine for the access, morphine and croton-chloral for pain, and antidiathetics like mercury, iodides, etc., as indicated.

In headache due to eye-strain the local application of atropine to the conjunctiva often affords great relief. In immature cataract and spasm of accommodation, instillations of atropine solution are used with benefit. There is little danger of systemic poisoning from this local use of atropine, except in idiosyncrasies. If the solution is allowed to become alive with microorganisms and is used long, granulation of the eyelids may arise. This is prevented by employing solutions certainly sterile. Some persons are so susceptible to atropine that the skin flushes at the least contact with it. Sometimes the mydriasis persists for months instead of subsiding within a week.

The internal uses of atropine spring primarily from its power of paralyzing the peripheral nerve-ends. The difficulty of sharply differentiating the toxic from the medicinal dose, and the contradictory results, are the reasons this mighty medicament has not attained the notable place it probably deserves (Liebreich).

In painful affections of the skin, mucous membranes and muscles, atropine has been administered with success.

As a muscular relaxant atropine finds employment in spasmodic conditions, sphincter constrictions, spasm of smooth muscular fiber, especially circular, in œsophagismus, cardialgia; colics, intestinal, hepatic, renal and uterine; spasm of the neck of the bladder, of the uterus, of the vaginal and urethral orifices, and of the anal sphincter.

In all pathologic contractions or excessive activity of non-striated muscle-fiber, in the tenesmus of dysentery, and in nocturnal enuresis, the use of atropine is well established; especially in lead-colic, whose phenomena may be completely dissipated by atropine (Harnack). By relieving spasmodic contraction of the muscular coat of the bowel, it relieves obstruction. Hence, in strangulated hernia it has been given with most satisfactory results. Oppenheider gave it in nine cases of obstinate painful constipation from hepatic cancer, peritonitis, etc., and obtained relief from full "toxic" doses. Norman Kerr reported five similar cases, three having fecal vomiting, all successful. It is indicated in all cases of high-grade, persistent constipation, where enemas and saline cathartics

fail and drastics cause pain; also where opiates and chloral have been used to relieve pain (Oppenheider). In this category come many cases usually ranked as appendicitis of the catarrhal form, and obstructions following the ingestion of indigestible food, such as berries, in very large quantities. Too many of these are subjected to the knife, too many die after the action of violent cathartics; but such cases yield readily when brought under the influence of atropine, with hot colonic flushing and saline laxatives.

Dyattschenko pronounced atropine inefficacious or dangerous in intussusception and volvulus, of little effect in dynamic ileus, especially with complete paralysis of a portion of the bowel, and only indicated in connection with electricity and massage.

Le Grix found this failure not surprising under the incompleteness of the treatment employed. When atropine and strychnine are employed together marvelous effects are obtained in treating the different forms of internal strangulation. When spasm of the bowel is present atropine will unlock this spasm; if there is paralysis, strychnine will restore the fibers to tonicity. If both are present, both remedies are indicated. But if the obstruction is not due to either of these conditions, neither remedy will give relief.

In six cases of incarcerated hernia Otermaier saw spontaneous reduction of four, after one hypodermic of atropine, gr. 1-67. In the other two cases reduction took place after the second or third similar injection. Experiments of Pal led him to conclude that atropine acted on the nerve-ends of the pneumogastric and splanchnic, the intestinal muscles and motor ganglia being unaffected. Muscular tone diminishes and the intestines are less excitable. Atropine is therefore useful only when the intestines are irritated by the way of reflex as in ileus. Mechanical stenosis is not amenable to atropine.

Rarely do these states depend on one morbid factor alone; so that with atropine we associate strychnine or brucine as general incitants, morphine and cicutine to subdue nervous hyperesthesia, and other agents in combating various phenomena.

In the convulsive stage of whooping-cough, in spasmodic asthma and all irritative coughs, atropine prevents the spasm. It finds application as an antispasmodic in dysmenorrhea, uncontrollable vomiting, volvulus, invagination and strangulated hernia.

In all these conditions atropine requires the aid of modifiers: Calcium sulphide, apomorphine, and quinine hydroferrocyanate in whooping-cough; strychnine and arsenic in asthma; ergotin,

iron, quinine, strychnine, in dysmenorrhea; brucine, strychnine, morphine for vomiting; strychnine for intestinal strangulation.

Atropine serves well for constipation or for diarrhea. By relaxing intestinal spasm it reestablishes the regularity of the evacuations; by arresting exaggerated peristalsis and glandular secretion it arrests intestinal fluxes.

The property of moderating secretion has been utilized in the night-sweats of phthisis, exaggerated salivation, bronchorrhea, diarrheas, and some claim in lactorrhea. Ebstein obtained good results in the salivation of a hemiplegic. In phthisis atropine combats the sweats, the diarrhea and the cough. In bronchorrhea it calms the cough, lessens the reflex irritability of the mucosa, checks the hyper-secretion and acts as an antispasmodic. In incontinence of urine it lessens the hyperesthesia of the vesical mucosa. It subdues the irritability of the urogenital mucosa in spermatorrhea.

In the choleras, Asiatic, infantile and morbus, Brunton had pointed out how exactly atropine antagonized the pneumogastric irritation constituting the disease, and Hankin first proved the truth of the deduction by using atropine in Asiatic cholera with remarkable success. In cholera infantum a hypodermic of atropine, suited to the age, gives speedy relief; but should not be relied upon to the neglect of intestinal antisepsis.

Its sensory-paretic action renders it of value in neuralgias and in some neuroses: trigeminal, odontalgia, otalgia, sciatica, epilepsy, chorea; in neuralgia, combining with morphine, strychnine, quinine, aconitine; in chorea with salicylates, arsenates, vermifuges, strychnine, brucine; in epilepsy with glonoin, cicutine, verbenin.

Atropine valerianate has been recommended in epilepsy by Schroeder van der Kolk and many others; but not in *grand mal* due to sexual excitation.

In eclampsia and hysteric spasms it has been administered with varying results. When glonoin is given in the first stage of epileptic spasms to dilate the cutaneous vessels, atropine should be added to prolong the effect.

Of late atropine has been very largely used to supplant opium as a remedy for pain. So many varieties of pain being amenable to atropine, and the danger of forming an atropine habit being absolutely *nil*, the tendency is to be favored. In neuralgias, the pallid, shrunken skin, contracted pupil, weak, repressed pulse, are directly antagonized by atropine, which recalls the blood to the surface and relieves the internal congestion. In spasmodic pains of every description, atropine is also the direct physiologic remedy.

In hemorrhages of every variety atropine has proved one of the most powerful hemostatics. A full dose should be given at once, hypodermically, enough to flush the skin. If the blood be withdrawn from the bleeding vessels to the skin it is necessarily out of danger.

During the past two years the writer has repeatedly advertised for reports of failure on the part of atropine to act as a hemostatic. One report was received, where a fatal hemorrhage occurred from the erosion of a pulmonary artery in rapidly spreading ulceration in an advanced stage of phthisis. One other failure was reported in typhoid ulceration. These were all. Reports were received of success with atropine in every known form of hemorrhage, active and passive, traumatic and hemophiliac.

H. W. Sigworth of Iowa says he always uses atropine after confinement where bleeding seems profuse, finding it handier, safer and more certain than ergot or any other hemostatic. He pronounces it a sure remedy in hemorrhage from the lungs due to tuberculosis, giving a granule of 1-250 grain every fifteen minutes. In a case of epistaxis in a boy of five years, when plugging the nose, tannic acid and adrenalin had failed, he gave two granules of atropine every fifteen minutes. The bleeding was controlled after the second dose.

Dr. M. B. Tuller, Kentucky, says that he has used atropine with favorable effect in hemoptysis. He gives it first, in all cases of uterine hemorrhage, when ergot fails; second, in menorrhagia and metrorrhagia, he has used it with apparent success, giving it in all such cases in preference to ergot. He also gave atropine in a case of hemorrhage in which abortion was suspected and examination refused. The hemorrhage ceased and the embryo was probably expelled by the oxytocic effect of the drug.

Many persons can break up a commencing acute catarrh by taking a full dose of atropine.

In combating morphine poisoning atropine should be given in doses of Gram 0.002 (gr. 1-30), repeated hourly until symptoms of atropinism are manifest, such as dry mouth, reddening face, bright eyes, dilating pupils. Beyond the beginning of toxic action it is unsafe to go, as the antidotal effects of atropine do not cover the entire range of the action of morphine. And in poisoning by the galenic preparations of opium it is well to remember that the convulsant effects of atropine may be aided by an unusual proportion of the tetanisant alkaloids of opium, thebaine, laudanine, etc. The cardiac and respiratory depression of opiates is antidoted by

atropine, and its use is to be directed solely against these features of opium poisoning, and not against the somnolence. Ignorance of this has occasioned many deaths.

Atropine is indicated in the cerebral inflammations with retarded pulse, and in eruptive fevers with delayed eruption and evidences of a nervous system overwhelmed by the onset of the malady.

In grave collapse in any form of narcotic poisoning its property of allaying the excitability of the cardiac vagus extremities can be utilized.

As an oxytocic atropine may be employed alone or combined with ergotin, quinine, strychnine or macrotin.

Administration.—It is in all cases best to administer atropine by the intensive method. The dosimetric granules are all too large for accurate dosage. One containing gr. 1-1000 would be preferable. Of these one may be given to an adult, best in solution, every five to twenty minutes, according to the urgency of the case, until the first evidence of action is manifest. This is almost invariably dryness of the mouth; only exceptionally do any of the classic symptoms precede this. When this dryness is felt it is time to stop the drug, as the full benefit has been secured, and if full relief has not ensued, some other remedy or surgical intervention is needed. This does not apply in poisoning cases.

Children bear atropine well, in larger doses proportionally than adults, but not all children. Double the dosage by Shaller's rule with all but flaxen blondes, and halve it with them.

When the dose for a patient has been determined with accuracy this may be given with advantage at once, especially when dealing with neuralgias and neuroses, where it is an advantage to deal a staggering blow to the malady at the outset, and timid medication will fail. So in urgent cases, cholera, colics, etc., it may be best to give a full dose at once.

Van Renterghem's advice as to adjuvants and combinations, given above, can be largely extended, by adding any other remedy indicated in each particular case. Obviously, we can only supply the ingredients and general directions. Whether the cake will turn out satisfactorily must depend on the cook.

Liniments containing atropine are usefully applied to the soles of the feet in hyperidrosis. Atropine represses the secretion of milk when applied to the breast. The local uses of atropine are as legitimate in liniments and plasters as in solutions applied to the eye.

Atropine is rapidly excreted by the kidneys. It enters the milk and the fetal circulation, and should not be given to a nursing mother.

In poisoning by atropine, the convulsions may be controlled by ether, the heart and respiration sustained by caffeine. Recovery is the rule.

Death has resulted from the use of Gram 0.12 (gr. 1 5-6) of atropine internally, and in the case of a consumptive, from a dose of only Gram 0.04 (gr. 2-3).

Appended is a list of maladies in some phases of which atropine has proved of benefit:

Therapeutic Summary.—Abortion: Increases uterine contractions and checks hemorrhage.

Abscess: Apply locally to abort by vasodilation and relieve pain.

Acidity: Checks hyperchlorhydria.

Acne: For greasy skin with free sweating.

Adenitis: Locally, relieves pain and favors resolution.

After-pains: Steady contraction relieves pain.

Alcoholism: The basis of all secret cures; the fullness of the head which it causes renders the liquor effect disagreeable.

Aphonia: The hysteric form has been relieved by full doses.

Asthma: When the skin is cool and moist, sputa loose.

Bladder, Irritable: Sedates irritability, checks nocturnal enuresis.

Boils: Applied in plaster, relieves pain and hastens maturation.

Bronchitis: To check profuse mucous flow, bronchorrhea, to relieve irritative cough.

Calculi, Biliary: To relax spasm of ducts and let stone pass, easing pain.

Calculi, Renal: To relax spasm of ureter and allow stone to pass.

Cataract: Immature forms benefited by instillations.

Catarrh, Acute Nasal: To abort the attack and dry up secretion.

Cerebral Anemia: To increase temporarily the cerebral blood-supply.

Cerebral Congestion: For less active forms of hyperemia.

Cholera Asiatica: Directly opposes the vagus irritation indicated by symptoms, for cramps, pain, diarrhea.

Cholera Infantum: Same as preceding.

Cholera Morbus: Same as preceding.

Chordee: Relieves all but febrile cases.

Chorea: For cerebral anemia, as antispasmodic, as hypnotic in small dose.

Colic, Intestinal: Relieves spasm, pain, constipation.

Colic, Lead: The best remedy for pain, spasm, obstruction.

Constipation: Very small doses paralyze inhibition, allay spasm.

Convulsions: For congestive, teething or whooping-cough forms.

Cough: Spasmodic, nervous, sympathetic, asthmatic, allays irritation.

Croup: Relieves irritation and stimulates respiration.

Cystitis: Relieves irritability, breaks up attacks due to catching cold.

Delirium: Relieves that of cerebral anemia.

Delirium Tremens: For insomnia with cyanosis, cold skin, coma vigil.

Dementia: Stimulates cerebral circulation, relieves insomnia.

Dengue: For sweating stage, when excessive or weakening.

Dentition: For the convulsions.

Diabetes Insipidus: Checks excessive flow.

Diarrhea: Checks excessive flow, choleraic, colliquative, irritative.

Diphtheria: Given early, aborts exudation, later to sustain heart, when throat and tonsils are acutely inflamed and swollen.

Dysmenorrhea: For spasmodic or neuralgic cases, dark fetid or profuse discharge, crampy pains and chills.

Dyspepsia: To relieve constipation and gastralgia, check hyperchlorhydria.

Dyspnea: Relaxes spasm.

Dysuria: For strangury, bloody urine.

Eczema: For eczema of the hand.

Emissions: For atony and relaxation of genitals, both sexes.

Emphysema: Relieves the dyspnea.

Enuresis: Nocturnal, of children, full dose at bedtime.

Epilepsy: For nocturnal, too sound sleepers, *petit mal*, to dissipate cerebral anemia of first stage.

Erections: Are strengthened by full doses and fear is allayed.

Erysipelas: Superficial non-vesicular forms, adynamic, phlegmonous or cerebral.

Erythema: To wind up protracted attacks.

Eye Affections: Especially for iris maladies.

Feet: For fetid perspiration.

Fevers: For delayed eruptions, insomnia and low delirium, photophobia, hebetude, hemorrhages, to sustain heart.

Gastralgia: To relieve neuralgic pain.

Gastric ulcer: To stop pain and vomiting, check acid production.

Glottis, Œdema: It may prove capable of drying up the effusion.

Gout: Very effective in relieving pain of gout of stomach.

Hay Fever: By drying up the secretion gives temporary relief.

Headache: Breaks up attacks in excessive meat-eaters. For pain over eye, photophobia, intolerance of noise or motion, uterine, gastric, in young women; face pale and skin shrunk, pulse small and contracted.

Heart disease: For irregular rhythm, cardiac strain.

Hematemesis: Full doses stop bleeding.

Hemoptysis: In full doses probably the best, strongest and quickest.

Hemophilia: Success reported recently in checking this.

Hemorrhage, Rectal: Has been highly recommended.

Hemorrhage, Puerperal: The quickest, strongest, best hemostatic.

Hemorrhoids: To stop bleeding and relax spasmodic sphincter.

Hernia: To relax strangulation, full doses.

Herpes Zoster: To relieve pain:

Hiccough: Full doses, to relieve spasm, with strychnine to steady nerve.

Hypochondria: For cerebral anemia, general relaxation, sexual atony.

Hysteria: For convulsions, aphonia, puerperal forms.

Impotence: To strengthen erections and relieve nervous dread.

Influenza: For headache, acute attacks, free sweating or other discharges.

Insomnia: For prostration, low arterial tension, contracted pupils, frontal headache, over-use of eyes.

Intestinal Obstructions: Full doses to relax spasm and relieve pain.

Iritis: Dilate the pupil fully, by local or general use.

Keratitis: If ocular tension be low, contracts vessels, limits inflammation.

Labor: Stimulates uterine contractions, lessens pain and bleeding.

Lactation: Checks flow of milk. Affects nursling.

Laryngismus Stridulus: Cuts short the paroxysm.

Locomotor Ataxia: Recommended by Brown-Séquard.

Lumbago: A hypodermic relieves acute attacks.

Mania: Allays irritation, induces sleep, quiets delirium, for nymphomania, hypochondria, delusions of persecution, whenever it is desirable to stimulate the cerebral circulation.

Mastitis: Relieves congestion and dries up milk.

Measles: Depression of vital powers, low temperature, delayed eruption.

Melancholy: For constipation and low arterial tension.

Menorrhagia: The best of the hemostatics.

Myalgia: Hypodermic to abort acute attacks.

Myelitis: For traumatic cases and anemic conditions.

Nephritis: For irritation and pain in kidneys in acute form.

Neuralgia: Full dose at once to break up attack. Sciatica, lumbago, uterine, ovarian, intercostal, dysmenorrheal, tic, spinal irritation.

Obesity: To check excessive sweating.

Oesophagismus: To relax spasm, ease irritable stricture or ulcer.

Orchitis: As soon as the acute symptoms subside.

Otalgia: For children, with coryza.

Otitis: To relieve pain.

Ovarian Neuralgia: The best remedy, says Waring.

Paralysis: For chronic myelitic paresis.

Perspiration: For phthisis, debility, relaxation of weak children.

Pertussis: To abort attack in incubation, check spasm and secretion.

Pharyngitis: Relieves pain and fever, aborts attack.

Photophobia: Dilate the pupil.

Phthisis: For colliquative sweats, diarrhea or bronchorrhea, irritative cough, dyspnea.

Pleurodynia: For all but rheumatic or uterine forms.

Pneumonia: In the first stage, infants, to check secretion.

Prostatorrhea: To check discharge and subdue irritability.

Pruritus: For obstinate cases and those due to sweating.

Rectal Ulcer: Relieves pain, especially burning after stools.

Rheumatism: Excessive sweating may demand atropine.

Roseola: For the sore throat and sweating, delayed eruption.

Scarlatina: To bring out delayed eruption, for sore throat.

Sciatica: Hypodermic down to sciatic notch.

Scurvy: For excessive salivation or relaxation.

Sea-sickness: Empty bowels and bring under atropine to prevent attack.

Sneezing: Dries up secretion and allays irritability.

Spasm: For local muscular spasm of sphincter, hysteric, anemic, spasm of teething.

Spermatorrhea: For relaxed genitals, nocturnal emissions, no orgasm.

Sunstroke: For heat exhaustion, all cases with low arterial tension.

Syncope: Give glonoin at once, with atropine to prolong cerebral hyperemia.

Tetanus: Injected near wound has cured.

Tonsillitis: With aconitine used early will abort attack.

Trismus: Inject into affected muscle.

Typhoid Fever: Contracted pupils, low muttering delirium, weak heart.

Ulcers: Has remarkably favorable influence over their course.

Urticaria: Gives temporary relief.

Variola: Low muttering delirium, prostration, delayed eruption.

Vomiting: Relieves that of pregnancy, if neurotic.

This list merely comprises some uses of atropine that are well known to every practician. Many others will suggest themselves to our readers, of equal importance with the foregoing. In truth, it is doubtful if any other single drug does as many things as this, and does them as well.

AVENINE

Standard granules—gr. 1-67, Gm. .001 of the alkaloid; gr. 1-6, Gm. .01 of the concentration.

Merck lists avenine, an alkaloid found in small proportion in the common oat. Avenin is a body resembling legumin, containing seventeen parts of nitrogen to one of oxygen. The entire plant is crushed to a pulp when the grain is in the milk, and treated with strong alcohol.

Avenin was introduced by Benjamin Keith as a remedy for paralysis. He had suffered from this and found no remedy that proved of benefit until he tried avenin. He firmly believed in the efficacy of avenin and advocated it energetically. The writer prescribed avenin for a man who had had a stroke of hemiplegia some years previously. The patient took the remedy two weeks, and

reported no effects. In two weeks more he believed it was doing him some good. At the end of another fortnight he was sure of it, and continued to take the avenin for a year, firmly convinced of its usefulness. And this has been the general result of the writer's use of avenin in similar cases, though not without exception. Just wherein the benefit lay is unknown—the patients are sure of it, and prize the remedy, finding it a comfort and their unpleasant sensations relieved.

Avenin has been recommended as a remedy to ease the alcohol or morphine habitué on ceasing the use of his drugs. The writer has tried avenine, avenin and Keith's tincture in alcohol and morphine cases, and found some benefited, but the majority obtained no relief. It is worth trying, and generally forms an ingredient of the tonics used for this purpose.

Sometimes persons who are not ill complain of feeling languid and unrefreshed on rising in the morning. A small dose of avenine, five granules, in a glass of hot water on going to bed, will be followed by a sound sleep and a sense of rest and strength next morning.

King gives as the specific indications for avenine: Spasmodic and nervous disorders, with exhaustion; cardiac weakness; nervous debility of convalescence; spermatorrhea from the nervous erethism of debility; tensive articular swellings. A nerve tonic, stimulant and antispasmodic.

BAPTISIN

Standard granule—gr. 1-12, Gm. .005.

From the root of Baptisia tinctoria, wild indigo, are derived baptisin, baptin and baptitoxine. Schroeder pronounced the first and second inert, and his verdict has been generally accepted. He found baptitoxine tonic in small and highly toxic in large doses, hastening the respiration, exaggerating the excitomotor power and causing death by asphyxia.

Plugge claims that baptitoxine is identical with cytisine, ulexine and sophorine. Kobert found the symptoms of cytisine resembling somewhat those of strychnine, but with vomiting of centric origin; cytisine depresses the ozonizing property of the red blood corpuscles during life; it excites and then paralyzes the respiratory center; powerfully stimulates the vasomotor centers, producing marked elevation of blood-pressure independent of the heart, followed (after large doses) by fall of pressure from vasomotor center paralysis. The motor tract of the spinal cord is strongly excited by small doses. paralyzed by large ones. The peripheral ends of the motor nerves

are paralyzed as with curarine. Cytisine also stimulates the uterine muscle and has often produced abortion.

Cytisine has been recommended for paretic migraine and cardiac dropsy, mucous irritability, nervous dyspepsia, restlessness from mental overwork, and frequent vomiting from slight excitation.

Specific Indications—Ellingwood says that baptisin is a bitter glucoside, baptin a purgative glucoside, and baptitoxine a toxic alkaloid. Specific indications for baptisia are: Mucosa of mouth dark, purplish; tongue, dry and thin with dark coating; face dusky and suffused; circulation feeble. Baptisin has a dynamic influence on the intestinal glands, antagonizing disease influences there, reinforcing the blood, preventing destruction of the red corpuscles and stimulating the removal of debris. In malignant tonsillitis and diphtheritic croup, and in phagedena tending to gangrene, it has proved curative. It is useful in dysentery with offensive breath and prune-juice stools; and in scarlet fever, when the specific indications above-described are present. In low fevers baptisia sedates the fever markedly, and soothes cerebral excitement.

Scudder gives as indications for baptisia: face full, dusky, purplish red, like one who has been in the cold for a long time; tongue the same dusky, purplish color; headache dull, pulse oppressed. This condition is met in zymotic and other maladies. The pulse is fast, fever high, the ordinary sedatives and baths do not have their usual effects. The pulse and fever fall under baptisia. Continued, scarlet and typhoid remittent fevers, dysentery and diarrhea, furnish indications, often on the first day. When gastrointestinal inflammations tend to necrosis or gangrene, baptisia enjoys high repute. It is a useful gargle in some throat diseases, the malignant forms of scarlatinous, variolous, diphtheritic and mercurial sore throat, and ulceration. Topically it is also applied to syphilitic ulcers, white swellings, "fever sores;" phagedenic, foul, fetid and gangrenous ulcers, sore nipples, chronic and scrofulous ophthalmia, fetid leucorrhea and genital ulcers. It is a local tonic and excitant to the vessels and tissues. It should be given internally at the same time. Cloths saturated with a strong decoction should be applied to the abdomen.

Webster terms baptisia a dynamic antiseptic and antizymotic, not acting chemically but by stimulating the vital functions. This is especially true of the intestinal glands, and also of the blood in septic and epidemic maladies. It is also useful whenever there is a

tendency to gangrene. Prune-juice expectoration in pneumonia is an indication. He reports a case of ischiorectal cellulitis with gangrene and systemic toxemia, recovering under baptisia and rhus tox.

Brunton classifies baptisin as a hepatic stimulant of secondary power, and says it also stimulates intestinal peristalsis.

Bocquillon-Limousin states that baptisin is used in France for erysipelas and affections of the liver.

Liebreich says baptisia is employed in Germany as a protective against horse-flies.

Webster suggests the use of baptisia in mania, melancholia and dementia, with stupor, and in all affections characterized by drowsiness or typhoid states.

The conflicting reports as to the effects of baptisia are probably due to varying proportions of the three diversely endowed active principles. Among the Eclectics, not only with the three authors quoted, but in numerous magazine articles, there is a remarkable unanimity as to the value of this plant and the uses to which it is put. It must be noted that by them it is invariably used in small doses, from one-fourth to five minims of the specific tincture, which corresponds to the fluid extract in strength.

The conditions in which baptisia is used are those in which the vital powers are overwhelmed by septic poisons, either in the whole body or, more commonly, in a part. Hence, when reaction appears deficient, when the systemic powers are not able to throw off the disease unassisted, and death of the threatened part is impending, baptisia is prescribed with the utmost confidence. The action, therefore, is analogous to that of capsicum or sanguinarine in pharyngitis.

It will be time enough to deny the possibility of such an action, when we know just what constitutes vitality, and the laws that govern it. Meanwhile, the important question is simply whether these assertions are founded on fact. Sometimes a man makes an observation—certain phenomena appear, a drug is given, and recovery ensues. He credits the drug with the cure, and many other physicians employ it in similar cases. Successes are reported, failures are not. And so the repute of the drug as a remedy is made—and yet the whole sequence was coincidental, not consequential; and an error is engrafted on medical practice, that may cost hundreds of mistakes and many lives before it is detected and corrected.

On the other hand, the presumption in such cases is in favor of a principle whose correctness is attested by many men. I have

been unable to find in my therapeutic library any record of a real trial given by the regular medical school to baptisia; nothing but the distrusting, slighting tests, ready to accept the slightest excuse for dismissing them with the contempt usually accorded remedies emanating from irregular sources. If the drug really possesses the properties claimed, it will be indeed a valuable addition to our resources.

In baptisin we have a useful bitter tonic resembling quassin, in baptin a cholagogue, one of these also stimulating peristalsis. Baptitoxine is probably the most important ingredient, to which the vital incitation is to be attributed. It would be interesting to note the effect of this upon the leucocytes. Whether depression of the ozonizing capacity of the red blood corpuscles interferes with bacterial operations, is a question for the future; but there can be little doubt but that the powerful stimulation of the vasomotor centers is indicated when vital depression threatens life. The spinal motor excitation it exerts also has its use. It is also noteworthy that the vasomotor excitation manifested by this remedy is altogether independent of any action upon the heart.

While baptisia is ranked by the eclectics among the antiseptics, its action is radically different from that of the chemical disinfectants. Baptisia enhances the vitality of tissues threatened with destruction, enabling them to resist the tendency to death. So far as we know this claim has not been made for any other remedy except echinacea. If true, we have in baptisia an agent whose value could scarcely be overestimated. Its field would include all the maladies in which danger may arise that the vital forces may go down under the onslaught of overwhelming numbers of the invading disease "germs," such as those of erysipelas, diphtheria, typhoid fever, smallpox, scarlet fever, measles, phagedena, dysentery, cerebrospinal meningitis, all affections characterized by ulceration, suppuration or gangrene.

Merck lists Baptisin, pure, purgative in large doses, tonic-astringent in small; dose Gram 0.032—0.3. Also Baptisin (Eclectic), dose Gram 0.05—0.52.

BARIUM CHLORIDE

Standard granule—gr. 1-6, Gm. .01.

The salts of barium were popular a century ago as remedies for scrofula, syphilis, heart-diseases and aneurism. In Italy they are given in chorea major and tetanus. Brown-Séquard recommended them for paralysis agitans.

Physiologic Action.—Barium chloride stimulates the intestinal motor ganglia, causing powerful peristalsis, even cramps, choking, dysenteric stools and vomiting. The blood-pressure is increased by contraction of the peripheral vessels, then falls below normal. The pulse is first rapid and irregular, then slow, ending with heart-paralysis and asphyxia. Respiration is labored. Tinnitus, diplopia, cramps from irritation of the medulla, and paralyses, indicate the effect of barium on the nervous system. Autopsies reveal inflammation and ecchymoses in the stomach and bowels. Barium has been detected in the blood, urine, spleen, liver and kidneys. The fatal dose for man is from Grams 4.0 to 10.0 (1 to 2 1-2 drams). Death does not occur for several days after the fatal dose has been taken.

Sollmann says that barium acts on the heart muscle, and causes strong vasoconstriction by direct stimulation of the muscular elements of the arterial coats. It is locally irritant, and inimical to the lower forms of life, such as yeast cells. He gives as the fatal dose of its salts 3 to 15 grains. The chemical antidotes are the sulphates which form insoluble combinations. This action on microorganisms might be utilized in combating sarcinæ were it not that the toxic dose is so near the therapeutic. Carbonated waters also precipitate baryta or barium oxide. (Laura).

Cushny says that in lethal doses barium chloride stimulates the spinal cord and the medulla, causing violent tonic and clonic convulsions. It causes very active peristalsis, and increases the blood-pressure enormously. Its effect on the heart muscle is antagonized by potassium salts. Barium is partly stored in the bones, partly excreted in the urine and the feces.

When used in medicinal doses for prolonged periods, chronic toxic symptoms may occur, such as nausea, diarrhea, catarrhs, cardiac and nervous depression. Barium seems better tolerated in hot climates. In the north daily doses of Gram 0.3 (gr. v) have caused unpleasant symptoms.

Pesci concludes that barium chloride acts as a muscular excitant, the therapeutic dose being four grains a day, this causing in man an increase in arteriole tonicity. It acts profoundly on the myocardium and arrests the heart in systole. Its influence is exercised directly on the muscle without the intervention of the nervous system. In these doses it is well tolerated and may be given for ten days at a time, the dose being gradually increased to one and one-half or two grams daily, without causing nausea or vomiting like caffeine, gastrointestinal disturbances like digitalis, or renal

troubles like calomel and the balsams. He calls attention to the possible danger of unduly increasing the blood-pressure, and especially advises its use in pleuritic effusions, in which he considers it the best or most inoffensive diuretic.

Schedel reports that in doses of 1-2 to 1-3 grain twice daily barium chloride increases vascular pressure, considerably reducing the pulse which becomes stronger and its tension noticeably greater. The effect lasts three days. The remedy exerted its effect where digitalis had failed. Epstein corroborates these statements, after many years' use of this remedy. Hence, while useful in anasarca it is perious if vascular tension is high.

C. D. F. Phillips recommends as a proper dose 1-16 to 1-12 grain three or four times a day, and considers such doses safe. Murrell says the symptoms following a toxic dose are pain in the stomach, purging, vomiting, anxious face, pulse feeble, breathing short and labored. There may be giddiness, cramp, paralysis and convulsions; collapse ensues, and death may follow. Phillips says that the small doses he recommends stimulate the stomach, increase the appetite and produce loose stools. Larger doses are irritant or caustic. The heart-action is at first stimulated, afterwards quickly and powerfully depressed by full doses. Small doses raise blood-pressure, while large doses cause a transient rise, succeeded by a fall, or if the dose is large enough a sudden fall at the beginning.

Da Costa praised it highly in restoring compensation and lessening cardiac pain; giving 1-10 grain three or four times daily for three weeks. Carpenter advised that this drug be used with caution, since a patient had alarming symptoms following 1 1-2 grains taken three times.

Flint gave it for fusiform aneurism of the abdominal aorta, gr. 1-5 three times a day. Improvement began within a fortnight and a cure was completed in five months. Prolonged rest and rigid diet were also employed.

The dose of barium chloride may be taken as gr. 1-6 repeated every hour till the desired effect has been obtained. This is better than the doses recommended by the textbooks, which are so different as to indicate considerable variation in the purity and strength of the specimens found in the shops. The dose of barium chloride usually advised is Gram 0.03 to 0.12 (gr. 1-2 to 2), three times a day.

Toxicology.—Barium carbonate is used as a rat poison. It is converted into the chloride in the stomach.

Quite recently it has been announced that barium is the toxic element of the plants whose consumption as food induces the famous loco disease of cattle and horses.

In poisoning with barium, empty the stomach by emetics and lavage, and give sodium or magnesium sulphate in large doses, to form the insoluble barium sulphate. Sustain the heart with cardiac tonics. Ogier and Socquet reported the death of a man five hours after swallowing 20 Grams of barium chloride.

Therapeutics.—Liebreich pronounces barium valueless in sclerosis of the nerve centers. Barium sulphate is an ingredient of depilatory powders.

Brunton recommends the chloride as a rapidly acting heart-stimulant, steadying cardiac rhythm and increasing the volume and force of the systole.

Epstein has given it in hypertrophy of the heart with abdominal aneurism, with excellent results.

Barium chloride has been especially studied by Hare. He finds that it slows the heart, steadies its rhythm, increases the quan tity of blood propelled by each systole, and raises the arterial pressure by acting on the muscular coats of the blood-vessels. In toxic doses it causes overstimulation with systolic contractions, the vagi not being paralyzed but overcome by the powerful cardiac contraction. He advocates this agent in all forms of failure of the cardiac muscle, and in varicose veins, the muscle-stimulation extending to the veins as well as the arteries. Barium does not cause the tense pulse of digitalis, the pulse-wave of the former being more prolonged.

BAROSMIN

Standard granule—gr. 1-6, Gm. .01.

Barosmin is a resin derived from buchu. This plant has had quite a reputation as a remedy for chronic inflammations of the genitourinary tract, irritability of the bladder, uric acid deposits, chronic urethritis, the incontinence of diseased prostate, especially profuse mucous or mucopurulent discharge with vesicorenal irritation (Felter-Lloyd).

It is indicated when the irritation depends on altered secretion from the urethral glands. Acid urine and incessant calls to empty the bladder with little relief, call for barosmin. Catarrh of the bladder from extension of gonorrhea or from irritant injections is relieved by it. For this condition and for long standing irritability with difficulty in restraining the flow of urine, Lloyd recommends the combination of buchu and iron. He gives as specific indications for

buchu: Abnormally acid urine, with constant desire to urinate, little relief following; vesicorenal irritation; copious mucous or mucopurulent discharges; cystorrhea.

The uses of barosmin are amply and better fulfilled by arbutin.

BEBEERINE

Standard granule—gr. 1-6, Gm. .01.

From the Nectandra, Pareira, Boxwood, Cissampelos and other plants, are derived alkaloids that are believed to be identical, and fully represented by bebeerine. This is extracted by a process similar to that employed for extracting quinine. Bebeerine occurs in yellowish amorphous masses, slightly soluble in water, freely in dilute acids, in five parts absolute alcohol or in thirteen parts of ether. The sulphate as found commercially is very impure, containing about one-third by weight of the alkaloid (King). It is presented as reddish-brown scales, soluble in water or in alcohol.

In its effects bebeerine closely resembles quinine. In small doses it is tonic, and in large ones antimalarial. It is antiseptic along the same lines, stopping the movements of the leucocytes and of lower organisms. It increases the appetite, relaxes the pulse a little, and in large doses causes ringing of the ears, and cerebral fullness, much as quinine does.

Laura says that toxic doses of bebeerine induce tetaniform convulsions, but it differs from strychnine in but slightly augmenting the spinal reflexes.

Therapeutics.—In malarial fevers bebeerine is useful but not equal to quinine. It has been praised in periodic headaches and neuralgias; especially those occurring in strumous and phthisical patients. It has proved effective in stopping the exhausting sweats of consumption. King recommends it for strumous ophthalmia, and as a useful tonic during pregnancy. Scudder praises it as a remedy for menorrhagia, when the flow is too frequent and too free. In leucorrhea also the tonic effect of bebeerine has been found equal to that of berberine. The dose as a tonic is gr. 1-12 to j, before meals; as a febrifuge and antiperiodic gr. v—xx. Boxwood has been used as an adjuvant to antisyphilitic mixtures, and with doubtful indication in epilepsy. In chorea, hysteria and chronic rheumatism its tissue-toning property may be of advantage. Berberine approaches most closely in action to bebeerine which seems to stand between berberine and quinine. In this day of accurate study of remedial agents, it should be ascertained if malarial spleens are contracted as well or better by bebeerine than by the hydrastis

alkaloid. In convalescence from malaria, and when quinine has not agreed or has lost its effect, bebeerine seems to be the logical substitute.

BENZOIC ACID

Standard granule—gr. 1-67, Gm. .001.

Benzoic acid is obtained from benzoin as a rule, or it may be made artificially from toluol. Benzoin, a balsamic resin obtained from Styrax benzoin, a tree indigenous to Java and Sumatra, is sufficiently common and inexpensive to render it undesirable to attempt sophistication to any great extent, and thus the larger part of the benzoic acid on the market—especially if prepared by a firm of repute—is the genuine product. As a matter of fact the artificial acid seems to answer every purpose though there is a great difference in the clinical results obtained from a number of samples. This perhaps is one reason for the widely differing opinions expressed by clinicians as to the value of this remedy.

Benzoic acid is found in many plants, free or combined with bases. It is also obtained from urine but it is impossible to prepare it so pure as to have no urinous odor. It may be obtained by oxidation from cinnamic acid, oil of bitter almonds, cymol, naphthalin, casein, glue, and other organic substances.

It forms loose, shining, yellowish or white crystalline needles or plates, of aromatic odor and sweetish taste, followed by a sharp, rasping. It is irritant if inhaled. The acid is soluble in 370 parts of cold and 20 of boiling water, in 7 of chloroform, 2 of alcohol, 3 of ether, 10 of glycerin, in carbon disulphide, and in turpentine. It evaporates with steam. Borax or sodium phosphate increases its solubility in water. Benzoic acid must be free from cinnamic acid, which when oxidized with potassium permanganate exhales the odor of bitter almonds.

Physiologic Action.—When benzoic acid passes through the body, it takes up amidoacetic acid, or glycocoll, and appears in the urine as hippuric acid. This takes place only under normal conditions of the kidneys; when they are disturbed benzoic acid passes unchanged. Part is eliminated by the lungs and the saliva in the form of benzoates and succinates.

Benzoic acid as an antiferment and antiputrefactive agent acts more powerfully than salicylic acid in some fluids, such as beerwort and putrefying flesh solution. This is because benzoic acid is more loosely combined with alkalies and more easily set free (Kolbe). One-tenth of one per cent of benzoic acid delays the

development of bacteria in a nutrient fluid, and two-hundredths of one percent hinders it. The propagation of bacteria is prevented by 3 to 4 per 1000 of benzoic acid (Bucholtz).

In man benzoic acid traverses the body in combination with alkalies, appearing free only in the urine. In the dog benzoic acid increases considerably the dissolution of albumin, without forming hippuric acid. If the doses are very large a reducing substance is formed, showing the body to be super-saturated, when the drug must be discontinued (Salkowski). Given internally in large doses to animals it produces paralysis, great lowering of temperature, the pulse and respiration being at first accelerated, then slowed, death finally supervening from respiratory paralysis. Benzoic acid is more irritant to the mucosa than salicylic acid, and in large doses causes nausea and vomiting.

Synergists.—As antizymotics, salicylic acid, carbolic acid, resorcin, the aromatics, thymol, volatile oils; while alkalies render the acid soluble and thus favor its passage into the blood.

Antagonists.—There are none; but acids and tannic astringents hinder the absorption of benzoic acid.

Therapeutics.—Van Renterghem thinks benzoic acid of advantage in asthenic pneumonias, chronic bronchitis and whooping-cough, as a stimulant expectorant.

In uremia, dropsies and eclampsias it stimulates the elimination of waste. While Huesemann does not accept Frerich's view as to the action of benzoic acid upon ammonia, he finds clinically that the acid is useful in nephritis. In conjunction with potassium acetate and chloroform the writer has employed this acid in desquamative nephritis, acute and chronic, for many years, with gratifying results. In fact, with the exclusive skim-milk diet, it has taught him to look upon this as a curable malady in the great majority of cases.

It is used as a dressing for wounds, as an inhalant in pulmonary gangrene and putrid bronchitis, and as an ingredient of cigarettes in asthma, chronic bronchitis and laryngitis. Twenty drops of tincture of benzoin in a pint of boiling water makes a good inhalation.

Frerichs urged benzoic acid in uremia, assuming that the ammonia developed from urea is neutralized and rendered harmless by this acid. This theory has not been confirmed by clinical observation (Penzoldt). Basing his recommendation on the antiseptic qualities of benzoic acid, and attributing the therapeutic efficacy of salicylic acid to this property, Senator advised sodium benzoate

in acute inflammatory rheumatism, especially when salicylic acid failed or disagreed. He advised the prolonged use of the remedy in large doses.

Benzoic acid has also been given in puerperal fever, gout and cholera infantum. Haberkorn urged its use in scarlatina and erysipelas, but experience has not supported the suggestion.

In pneumonia of the aged benzoic acid Gram 0.1—0.5 (gr. 1 1-2—7 1-2) is given with camphor, several times a day, and even up to ten Grams a day without harm (Liebreich). Iron benzoate is soluble in cod-liver oil, and is sometimes given in it.

For cystitis with fetid ammoniacal urine, Van Renterghem finds benzoic acid useful, but inferior to boric acid. Burggraeve employed benzoic acid because uric acid is replaced by hippuric acid, whose bases form in the blood extremely soluble salts.

Van Renterghem finds doses of three or four milligrams (gr. 1-20 to 1-15) sufficient to afford the benefit. In respiratory affections he combines strychnine arsenate or brucine; in grave fevers, typhoid, typhus and acute uremia, he has recourse to the defervescents, quinine, intestinal lavage with neutral magnesia salts; in chronic uremia he employs such special modifiers as the symptoms may indicate.

In urinary affections digitalin, hyoscyamine, cicutine, arbutin, cubebin and strychnine, can be called to aid benzoic acid in appropriate cases (Van Renterghem).

Bouchardat employed benzoic acid in gout, giving it in the form of a tisane containing a Gram to the liter. Rutherford pronounced sodium benzoate an excellent diuretic, stimulating mucous membranes in general. It also stimulates metabolism. Laura recognizes its applicability in the uric and hippuric diatheses, in gravel and gout; also in mild and chronic rheumatisms, adding lithia salts and securing "splendid success." Tordeus after many trials declared in its favor in whooping-cough and thrush. Leitzering and Kien approved of it in diphtheria. Here Laura adds calcium sulphide. Klebs recommended it in all infectious maladies, from their parasitic origin and the antiseptic qualities of the benzoates. Kroczac extended this application to tuberculosis itself. In vesical catarrhs Laura advised sodium benzoate with cicutine, hyoscyamine and also strychnine, to calm the spasmodic element and vanquish the paretic element present. Burggraeve and his associates limited their dosage to 10 or 20 granules a day, a centigram each. Of ammonium benzoate they advise similar doses, but on occasion run them up to 8 or even 17 grains a day.

Laura advises lithium benzoate when the salicylate is not well tolerated, and for rheumatism localized in single joints.

The great value of this acid and its salts is in affections of the urinary tract, as an antiseptic, soothing irritation, and under its administration bacteria disappear from the urine. It exerts a solvent action on calculi, of urates or phosphates. King says the indication for it is ammoniacal or alkaline urine, and that it only relieves rheumatism when the urine is alkaline. In nocturnal enuresis, dysuria, the dribbling of the elderly bladder, in gleet and in phosphaturia, it gives good results if the urine is alkaline. Wood affirms that under the use of this acid uric acid crystals rapidly disappear from the urine. Bird praises it in uricemia.

Locally, solutions of benzoic acid may replace the tincture of benzoin for freckles, pityriasis versicolor, moth patches, chronic urticaria, all sorts of itchings, for chaps, fissures, old sinuses, and as a styptic. As an application for unhealthy wounds and ulcers, the tinctures of benzoin have had a reputation for ages; but the wisest way to use them is as preventive of unhealthy states, by applying them to fresh wounds, when the benzoin forms a protective varnish over the exposed surfaces.

Shoemaker suggests the following application for freckles and moth: Corrosive sublimate gr. ss, tr. benzoin 2 1-2 drams, glycerin 2 drams, rose-water to make 6 ounces.

Ammonium Benzoate in small doses stimulates the circulation, accelerates the blood-current, and thus elevates the temperature and increases the secretions, especially those of the bronchi and the sweat glands. In large doses long continued it causes an aplastic state of the blood, with multiple hemorrhages, lesions of nutrition and profound debility. These neutralizing and antiseptic properties render it suitable in typhoid fever, while as a diuretic it relieves certain dropsies. It dissolves the concretions of uric acid, gravel and gouty tophi. As a stimulant and sudorific it is useful in atonic arthritics. It stimulates the bronchial mucosa in dry catarrhs. The dose is one to four centigrams (gr. 1-6 to 2-3) four or five times a day.

Lithium Benzoate.—Garrod exposed fragments of bone covered with urate of soda deposits to solutions of lithia, potash and soda; the first completely dissolved the deposits, the potash did so largely, the soda not at all. In gout lithium benzoate acts as an excellent diuretic; in uric gravel as a dialytic agent. The dose is the same as that of the ammonia salt.

Calcium Benzoate has been specially recommended as a remedy for albuminuria.

Sodium Benzoate occurs in white anhydrous amorphous powder, soluble in 1 1-2 parts of water, 45 of alcohol, 1.3 of boiling water, 20 of boiling alcohol. The antifermentive and putrefactive power of this salt is equal to that of the pure acid, or even greater (Bucholtz); as 5 to 6 parts to 10,000 prevent bacterial development.

Large doses cause trembling, convulsions and ataxic movements of the anterior extremities, progressing to complete paralysis; also vomiting and gastric hemorrhage, but no diarrhea. The pulse and respiration are first accelerated, then slowed. The temperature falls very low. Death occurs from respiratory paralysis. Sudden toxic phenomena appear in all animals experimented upon, if the dose exceeds 2-10 percent of their weight (Schulte). In man five Grams cause nausea and vomiting, preventable by strong exercise (Meissner). In addition a dose of fifteen Grams caused dizziness, rapid pulse, subjective heat, sweating and expectoration (Schreiber). In fever it is an excellent antipyretic.

Like benzoic acid, the sodium salt is used as a stimulant expectorant in catarrhs of feeble or aged persons, with little or no fever, the bronchi filled with secretions; also in pneumonias occurring in such patients. Nothnagel is skeptical as to its efficiency here, as well as in uremia, uricacidemia, erysipelas, diphtheria, typhus, polyarthritis rheumatica, cholera infantum, etc.

Sodium benzoate stimulates the action of the liver and increases the elimination of nitrogen by the kidneys. In some cases its use has occasioned erythema, papules, or urticaria.

Shoemaker speaks of its use in chronic diarrheas and dysenteries, indigestion from torpidity of the liver, and excessive uric acid excretion. As an antiseptic it has proved useful in acute rheumatism, septic fevers, scarlatina, variola, diphtheria, typhoid fever, whooping-cough and erysipelas. In rheumatism it disagrees with the stomach in large doses more than salicylic acid does.

Dosage.—Benzoic acid, Gram 0.05 to 0.5 (gr. 1 to 7 1-2) at each dose.

Sodium benzoate, Gram 0.5 to 4.0 (gr. 7 1-2 to 60).

These are the old-fashioned doses, designed to flush the system several times a day with a flood of the remedy. Under the dosimetric system it has been found better to keep up a continuous impregnation of the blood with the remedy, by giving small doses, about gr. 1-6 of either the acid or any one of its salts, every half-hour, or one or two hours, according to the acuteness of the symptoms it is designed to relieve. The efficiency of these small doses thus given, is readily demonstrated. In chronic maladies of the

urinary apparatus the administration should be continued for months, the necessary hygienic precautions being taken at the same time. When pus is passing in the urine at the same time, the addition of arbutin is advisable, and in gonorrheal infections the sulphides of lime and of arsenic may be added. In most forms of cystitis it is also wise to wash out the bladder with a saturated solution of boric acid, and inject a dram of Euarol three times a week. But the use of these accessory measures must not divert the attention from the persistent administration of the benzoates, from which so much may be expected.

BERBERINE

Standard granules—gr. 1-67, Gm. .001; gr. 1-6, Gm. .01.

Berberine is the most universally diffused alkaloid in the plant world. It is found in a multitude of plants such as columbo, the Berberidiæ, Menispermaceæ, Ononaceæ, Ranunculaceæ, Papaveraceæ, Rutaceæ, and Cæsalpineæ. Many of these plants have acquired repute as tonics, antiperiodics and astringents, etc., the larger part of the credit being justly due to the berberine contained.

The formula of berberine is $C_{20}H_{17}NO_4$. It is closely related to papaverine, narcotine and hydrastine. It forms yellow needles, insoluble in cold, soluble in hot water and in alcohol, insoluble in ether. Solutions are yellow, and very bitter. The salts are golden yellow. The acetate and phosphate are most soluble. They are more soluble in pure than in acidulated water.

Physiologic Action.—Berberine appears in the bowels, even if given subcutaneously, but not in the urine. It acts on the central nervous system (Falck), first paralyzing the automatic centers, then the spinal cord. In rabbits hypodermic injections of Gram. 0.1 of berberine sulphate cause death with paralysis of the hind legs, convulsions, falling of temperature, diarrhea, and weakening heart and respiration. Death is due to asphyxia, from paralysis of the respiratory center. If not promptly fatal, albuminuria occurs, the renal epithelium becomes swollen and turbid, even fatty. But Gram 0.8 given by the stomach is not fatal, but simply causes diarrhea, sometimes vomiting, tremor, rapid pulse and breathing and weakness. Its repeated administration produces anorexia and loss of weight. Increased peristalsis is noted even when berberine is given subcutaneously or injected into the bowel. In fatal cases the latter is strongly contracted. The spleen is contracted by berberine (Falck), and also the uterus (Fellner). Small doses lessen the irritability of the vagus and slightly hasten the pulse, followed

speedily by slowing, as the excitomotor ganglia's irritability is exhausted (Marfori). Fatality is due to heart-exhaustion. Small doses do not influence the blood-pressure but large ones lower it decidedly.

Berberine stops the movements of the leucocytes, while the red corpuscles become granulated and their contents diminished, the union of the oxygen with the hemoglobin becoming firmer.

Recovery from effects of overdoses of berberine is slow. The rapidity of the pulse appears to be due to paralysis of the cardiac inhibitory nerve-ends, and to the attendant fall of vascular tension; this effect being exerted on the vasomotor centers as well as on the heart. Very strong solutions exert an effect upon bacteria and upon the leucocytes analogous to that of quinine.

Berberine is in part excreted by the kidneys unchanged, the rest being broken up in the body (Cushny).

Brunton says that doses of Gram 1.0 (gr. 15) in man, taken by the stomach, cause only slight colicky pains and diarrhea. It lessens the oxidation of the blood.

Berg took Grams 3.6 (gr. 55) of berberine without any inconvenience, so that in man this agent is not lethal in any dose likely to be taken.

Therapeutics.—Many plants containing berberine are popular; columbo as a simple bitter, hydrastis as an astringent bitter, fraxinus as a contractor of tumors, xanthoxylon as a stimulant to unhealthy ulcers, etc. When there is a lack of tonicity in the intestines, with constipation or passive laxation, berberine is indicated. It has been found very effective in enlargement of the spleen. Curci praises it in chronic dysentery and gastrointestinal catarrhs, while Beil advises it in infants' diarrheas.

Fellner used it in menorrhagia, Maggiorani and others in chronic malaria, Vehsemeyer in leukemia. In menorrhagia berberine acts only by contracting the uterine tissue, especially in subinvolution; and is less effective than hydrastine, which is still inferior to hydrastinine.

Shoemaker recommends berberine for injection in gonorrhea; as a remedy for dyspepsia, malaria and atonic diarrhea. He attributes to it tonic, antipyretic, antiperiodic and cholagog properties.

Macchiavelli and Reil testify also to its value in malaria, giving Gram 0.12 to 1.0 (gr. 2—15) during the remission. Lascarato states that the contraction of the spleen caused by berberine is so powerful that over-doses may cause rupture of that organ, with

fatal hemorrhage. If the spleen is degenerated there is no action. This shows the radical difference between berberine, a contractor of connective and muscular tissue, and ergotin and digitalin, contractors of blood-vessels. Berberine is useless in hemorrhages. The difference between the latter and quinine is also shown by the access of fever following the contraction of the spleen by berberine; for the parasites are thereby simply extruded into the blood, not killed. Therefore, the treatment of malaria should include berberine to force the parasites out of the spleen into the circulation, and quinine and arsenic to destroy them.

The maximum dose of berberine in malaria is Gram 1.0 in 24 hours; but usually it suffices to give Gram 0.01 (gr. 1-6) every waking hour. In many other maladies Gram 0.001 every hour is sufficient; for berberine is emphatically a remedy for prolonged administration in minimal doses for chronic maladies. Thus given, its effects are notably persistent, sure and uniform.

Looking upon berberine as a stimulator of peristalsis and a contractor of relaxed atonic tissues, it has been extensively advised in cases of many diseases where the relaxation, atony or defective contractility of the tissues seemed to be a bar to the restoration of health. The results have justified the high expectations based on this agent. It deserves to rank among the most certain and generally useful of "condition-remedies," if I may be allowed to coin the expression, at our command. It is very slow in manifesting its effects, but once secured, they are permanent. In employing berberine to reduce dilatation of the stomach the diet should be carefully regulated and the stomach never once allowed to be distended by overfilling or to be chilled by iced drinks. It seems that an agent so frequently met in the plant world, and in such generous proportions, ought to be furnished by the chemists at a better price; and if its use continues to increase, it will undoubtedly become cheaper. But the best effects are obtained from small doses long continued, so that the unavoidable expense is well distributed.

The property of contracting connective tissue points to several other uses to which berberine could be put. In dilatation of the heart, without fatty degeneration, the use of berberine in conjunction with strict limitation of the use of fluids, is a far more rational procedure than the routine administration of digitalis. And in the enlargement of the liver that attends the advanced stages of valvular cardiac maladies, we have a field peculiarly fitted for berberine. If this drug contracts the liver as energetically as it does the spleen, its use should be exceedingly valuable.

BILEIN

An organ is "insufficient" when it no longer performs its functions properly. In the case of the liver with its manifold functions the character of the insufficiency varies greatly in different cases. Advanced degrees of hepatic insufficiency usually due to widespread destructive lesions of the liver parenchyma are, as a rule, easy to detect from their gross clinical manifestations; the incipient stages and milder forms are frequently overlooked; or, if detected at all they are often misinterpreted. Inasmuch as intelligent treatment is of the greatest value in curing hepatic insufficiency in its early stages, particularly those forms that are functional and are not due to progressive organic liver changes, and inasmuch as an intelligent prophylaxis in general prevents the occurrence of such an attack, even in predisposed subjects, it is of paramount importance to understand *first*, the causes that can produce these milder forms of hepatic insufficiency; *second*, the symptoms, direct and remote, that hepatic insufficiency produces, and, *third*, the best remedial measures, medicinal and otherwise, that can be employed to successfully combat the disorder when it first makes its appearance.

The causes of hepatic insufficiency can conveniently be classified under three heads: viz., (1) mechanical; (2) infectious (parasitic); (3) toxic.

1. *The mechanical causes* can be dealt with in a few words. They are characterized either by traumatic destruction of liver parenchyma, by overgrowth of interstitial tissue, causing mechanical compression and degeneration of functionating liver tissue, or by mechanical obliteration or obturation of blood vessels supplying large areas of the liver, with resulting death of many hepatic cells.

Among the mechanical causes that may further lead to hepatic insufficiency can also be classed certain heart lesions (especially tricuspid insufficiency) that produce venous stasis in the liver, and in this way interfere with the nutrition and the function of the liver cells and hence, indirectly, with the importation and exportation of the various bodies that are elaborated in the liver.

Finally, occlusion of the common duct, by whatever cause, also mechanically produces liver insufficiency. The high pressure in the labyrinth of bile capillaries that surrounds each islet of liver cells and the chemical irritation of the bile retained in these channels must needs cause degenerative and necrotic lesions of many thousands of liver cells, and hence seriously interfere with the functionating powers of the liver as a whole.

2. *The infectious* (*parasitic*) *causes* of hepatic insufficiency occupy an intermediary position between the mechanical and the toxic ones; in fact every parasite or microbe that invades the liver or its channels presumably acts both as a mechanical and a toxic cause, inasmuch as it primarily constitutes a foreign body, and hence an irritant in the liver parenchyma or the obturator of the blood-, bile-, or lymph-channels of the liver, and secondarily, in the majority of cases, elaborates chemical products that act deleteriously because they are toxic.

Almost any of the intestinal parasites (echinococcus, distoma, bilharzia, etc.), any amebic or bacterial microorganism circulating in the blood or lymph of the liver or entering the bile-ducts from the intestine or from the vessels of the peritoneum may produce organic liver lesions or functional insufficiency of the organ; and it would be a work of supererogation to enumerate all these parasites in detail.

3. *Toxic causes.* The most common and at the same time the least appreciated and least understood causes of liver insufficiency are toxic agencies of manifold origin. Their port of entry into the liver may be *via* the systemic blood- and lymph-channels that traverse the liver in every direction and carry a stream of blood and lymph through and around each hepatic cell, but the most common sourse of liver intoxication is the blood of the portal vein. When one remembers that the intestinal tract is teeming at all times with a superabundant flora of bacteria, many of them toxic; that the bowel is at all times filled with a decomposing and often putrefying and poisonous mass of albuminous, fatty and starchy material; and that the bulk of these degradation products must pass *via* the portal system through the liver, it will readily be understood that the liver, more than any other organ, is constantly exposed to toxic influences.

Normally the specific properties of the intestinal mucosa protect the liver from these poisons, inasmuch as this mucosa seems to exercise a selective affinity for the different ingredients of the bowel contents, retaining or disintoxicating the more poisonous products and permitting only the passage of harmless bodies into the radicles of the portal vein that conduct the blood from the intestinal wall to the liver; whenever the gastrointestinal mucosa, however, is diseased, as in many infectious disorders, after various excesses in eating and drinking, in catarrhal states, in certain nervous disorders, in chronic constipation, etc., or when especially virulent bacteria are swallowed and produce abnormal putrefaction in the

bowel, or when the bile-secretion is perverted or reduced or arrested so that the germicidal action of this secretion is withheld and the pullulation of enteric bacteria remains unchecked, whenever, finally, abnormal poisons are swallowed; then the portal blood becomes abnormally toxic and the liver cells, no longer able to adequately exercise their disintoxicating function, are overwhelmed by the broad stream of poison that swamps them; thus they become functionally impaired.

Again, when the physical characters of the bile are perverted, certain poisonous ingredients of the bowel-contents can, so to say, "back up" into the bile-channels and traveling against the sluggish bile-stream reach the liver-cells through this path. The liver-cells, it will be seen, therefore, are open to attack from all sides,—being amenable to damage from three distinct channels, viz., the blood-, the lymph-, and the bile-channel, and as they are practically swimming in the fluids passing through these three systems of capillaries, it is not surprising that any change in the composition of these humors must exercise a deleterious effect on the life of these cells and bring about insufficiency of their function.

In the same sense any derangement of the hepatic cells, whose chief duty it is to elaborate new products from the many bodies that circulate around and through them, whose main function it is to render harmful bodies innocuous by disintoxicating them, must invariably lead to a widespread distribution throughout the whole system and through these same channels and their many ramifications, of abnormal and poisonous products. *In this sense hepatic insufficiency becomes the chief cause of autointoxication.*

The symptoms of hepatic insufficiency are manifold. The most common sign of advanced insufficiency is icterus, or, better, cholemia, that is, the absorption into the blood-stream of bile-products that should properly be poured into the bowel. As a rule this diapedesis of bile from the bile- into the blood-channels of the liver is due to some mechanical obstruction of the bile ducts either from the impaction of a gallstone, or from catarrhal swelling of the larger bile-channels, or from viscidity and thickening of the bile in catarrh of the ducts, or from swelling of the intestinal mucosa around the orifice of the common duct. Generally speaking, this stasis and absorption of bile can never primarily be considered evidence of hepatic insufficiency *for the fact that the cells continue to exercise their normal function of manufacturing bile demonstrates that they are not insufficient.* Only when the pressure exercised mechanically on the cells and the hepatic blood-vessels interferes with the nutri-

tion of these cells do we, properly speaking, witness the signs of liver-insufficiency, and this becomes manifest by the retention in the blood and the appearance in the urine of those complex bodies that should properly have been elaborated in the liver-cells to form in part the constituents of the bile and in part certain non-toxic circulating bodies.

The physiologic evidence of liver-insufficiency can conveniently be summarized under five heads, viz.:

1. A reduction of the urea-forming function. Result: A diminution of the urinary urea; consequently, inasmuch as urea is the most potent physiological diuretic, a decrease in the amount of urine, and the flooding of the blood stream with the (toxic) precursors of urea (notably ammonia salts that fail to be elaborated into urea), and the appearance of these same bodies in abundant quantity in the urine. The impression made by these upon the nerve tissues induces a variety of phenomena.

2. Failure on the part of the liver to elaborate properly the sugars and starches that reach the organ from the bowel and the systemic blood. Result: The appearance of sugar in the urine (alimentary glycosuria) and the withdrawal from the muscles and the glands of their most important source of energy and heat-formation. And inasmuch as the organism is forced to consume its own tissues to make up for the deficit this produces, muscular lassitude and derangement of all the glandular functions and loss of weight.

3. Perversion of the bile-forming function with the consequences enumerated above, i. e., intoxication of the organism with products that should properly have formed bile, and absence of this important antitoxic, germicidal and fat-emulsifying secretion from the bowel with all the dire effects that the lack of bile can exercise on bowel-digestion, assimilation and general nutrition.

4. Loss of the general disintoxicating function of the liver. Result: Greater liability of the organism to a multitude of infections and intoxications, from germs and poisons invading the body from without and generated from within.

5. Insufficient elaboration of circulating albumins, fats and iron that should normally in part be disassimilated, in part be built up into complex molecules by the liver-cells. The incomplete metabolism of iron, by interfering with the proper formation and disintegration of hemoglobin and its derivatives, may become a very prolific source of anemia and of all the serious consequences, particularly in regard to oxidation, that this state engenders.

It appears unnecessary to discuss in detail all the manifold signs that may result from the impairment of these many functions. They are self-evident and vary greatly in each case according to the particular function or functions of the liver that may be impaired. One important point, however, remains to be emphasized and that is the common involvement of the kidneys in all cases of hepatic insufficiency. It stands to reason that the toxic circulating substances that the liver fails to eliminate into the bowel and the numerous toxic products that are formed by the faulty action of the liver-cells must seek an exit from the body by other emunctories. Chief among these are the kidneys, and it is not surprising that the delicate renal epithelia soon succumb to the extra work of ridding the blood of the mass of toxic bodies that clamor for elimination. The result is albuminuria and renal inflammation, followed sooner or later by renal insufficiency. As soon as this occurs the body becomes overwhelmed with poisons, the heart and arteries undergo degenerative changes, then arteriosclerosis, cardiac hypertrophy and the manifold consequences of cardiovascular disease and insufficient blood-supply to various vital organs supervene and such chronic disorders as Bright's disease, gout, diabetes, the uric-acid diathesis and many nervous disorders develop. That in the course of such a chronic autointoxication due to hepatic and renal inadequacy various skin eruptions must develop is not surprising when we consider that the skin must vicariously assume the elimination of the highly poisonous products that the liver and the kidneys can no longer get rid of.

This in broad outline is the symptomatology of hepatic insufficiency in its direct and remote consequences, and from its mildest and most transitory to its most severe and altogether irremediable consequences. The ancients and the laity of all ages were not altogether wrong when they attributed to insufficiency of the liver-function almost every ailment that human flesh is heir to—and this applies as well to bodily ills as to the disorders of the mind and the emotions. How wisely the ancient Greeks chose the terms melancholia and hypochondriasis and referred these depressive states, the "grouch" of today, to a deranged liver; for melancholia means literally "the black flow" and refers to disordered bile, and hypochondriasis means "under the ribs," and certainly incriminates the liver. And the wise physicians of all ages who have kept the bowels wide open and stimulated an active liver-function as a panacea for all ills were not far from right. They were good ministers to the sick.

If hepatic insufficiency is chiefly due to poisoning of the liver cells with various toxins, if these toxins are principally derived from the gastroenteric tract under the conditions outlined above, then five tasks of treatment at once become apparent, viz.:

1. To limit the ingestion of substances that either are toxic of themselves or that chiefly give rise to the formation of toxic degradation products in the bowel.

2. To prevent any abnormal putrefaction processes in the gastroenteric tract that may lead to the formation of these poisonous degradation products.

3. To prevent the absorption of these bodies from the bowel if they have been formed.

4. To destroy them as rapidly as possible if they are absorbed.

5. To promote the most rapid elimination of those toxins that cannot be destroyed in the tissues after they are absorbed.

While all the toxins that can disorder the liver cells are not formed in the bowel, but some, as set forth in previous paragraphs, are also manufactured in the tissues proper (as in certain infections and in certain obscure metabolic disorders), the same sequence of treatment must be adopted in order to neutralize their effects; the difference between the two classes of toxins considered as poisoners of the liver cells lies merely in the path by which they reach these cells, the bowel-poisons traveling by way of the portal vein and its liver capillaries, the tissue-poisons by way of the capillaries of the hepatic artery and the lymph-channels of the liver.

All this treatment, the details of which are to be given below, may be considered causal. In addition it is possible, as I will have occasion to show, to directly stimulate the liver cells when they become insufficient and in this way to aid them in resuming their normal function.

Finally many of the remote consequences of hepatic insufficiency call for symptomatic treatment. This applies in particular to disorders of the kidneys, of the heart and arteries and of the nervous system; for the renal, the cardiovascular and the nervous apparatus, it appears, bear the brunt of the general intoxication that follows inadequacy of the liver function. A discussion of these remote consequences of hepatic insufficiency and of their treatment will lead us, in later articles, to speak of some of the newer ideas concerning the nature and the treatment of arteriosclerosis, Bright's disease and an important trinity of metabolic diseases (that are in part based on neurosal disorders), viz.: diabetes, the uric-acid diathesis and obesity.

1. The elimination of toxic or toxicogenic (poison-producing) substances from the diet. Chief among these substances are alcoholic beverages; I intentionally say alcoholic beverages and not alcohol, because the latter, so far as the liver cells are concerned, is probably the least injurious ingredient of the former. Pure ethyl-alcohol, if taken in the dilution of ordinary alcoholic liquors, would never exercise the deleterious effects upon the organism as a whole and the liver in particular that we know liqueurs, cordials, cocktails, many wines and malted liquors, and many of the cheaper brands of whisky and gin to exercise. Ethyl-alcohol, i. e., the alcohol found chiefly in pure wines, is the least toxic of the whole group of alcohols, and others of the series that are found in the common beverages are infinitely more toxic; in addition these beverages contain very poisonous aldehydes—the latter bestowing the socalled flavor, aroma, "bouquet," to wines and other liquors—besides the aromatic oils of most cordials and cocktails, of gin, of absinthe (that contains no less than nine poisonous essences!) which are very injurious to the liver cells. Alcoholism, therefore, cannot be considered as ethyl-alcohol poisoning, but as a very complex form of chronic intoxication, the ethyl-alcohol, as such, affecting principally the heart, the arteries and the higher nervous centers; the various higher alcohols, aldehydes and the essential oils affecting principally the cells of the liver. Alcoholic beverages should, therefore, be rigidly excluded from the dietary of a sufferer from hepatic insufficiency.

To the category of liver irritants belong also most of the spices and condiments, flavoring sauces and most forms of cheese; all these articles should therefore be avoided because they contain poisons, preformed, that irritate the hepatic cells.

In selecting a diet for a case of liver insufficiency care should be exercised to exclude fats, as much as possible for these are poorly assimilated when the bile secretion—as a result of the hepatic disorder—is abnormal; they consequently remain in the bowel and rapidly undergo abnormal decomposition with the production of highly irritating and highly poisonous splitting products, chief among them glycerin and a variety of fatty acids; these are particularly harmful as they reduce the alkalinity of the bowel contents and hence interfere with pancreatic digestion. On a fat diet the toxicity of the urine always increases in liver patients.

Meats, as we know, contain many poisonous bodies; their use should therefore be limited, and much care should be bestowed upon the selection of the kind of meat and the mode of preparation.

Thus, it is known that raw, rare, cured and smoked meats of any kind contain a variety of highly poisonous, socalled extractives that can cause irritation of the liver, high blood pressure and nephritis; such meats, therefore, should be excluded. For the same reason, i. e., because they contain these extractives, meat extracts, meat gravies, bouillons, broths, etc., should be forbidden. All tainted meats, "high" game, etc., contain certain alkaloids that are very toxic, and should not be eaten.

A restriction of the amount of meat is always advisable in liver patients for the reason chiefly that the bowel always contains abnormal putrefactive bacteria that are normally held in check by the germicidal action of the bile but that can pullulate unhindered when the bile flow is decreased or the character of the bile is changed as in hepatic insufficiency. Even under normal circumstances meat forms certain degradation products in the bowel, socalled peptotoxins or ptomapeptones that are intensely poisonous when introduced into the circulation; when everything is well with the liver these bodies are arrested or disintoxicated in the liver cells and the organism is protected; when the hepatic cells become insufficient they not only favor the formation of an abnormally large quantity of peptotoxin in the bowel, owing to their inability to manufacture the proper kind and the proper quantity of bile, but they also become unable to arrest the large quantities formed, and hence allow self-intoxication of the organism. Meat, therefore, should be reduced.

The kind of meat is not so important as one was formerly inclined to believe; the difference as regards harmfulness between red and white, or dark and light meats is largely theoretical. The prejudice against red meat is widely disseminated, but I have never been able to convince myself that it is more or less harmful than light meat, nor do I find any valid evidence in the literature to induce me to exclude it from the bill of fare of my liver patients. The old empiric prohibition of red meats is borne out by experimental research and clinical investigation as outlined above, in speaking of the toxicity of the meat extractives that red meats contain. The preparation of the meat is important; it should be well cooked, i. e., boiled or broiled, but neither fried nor roasted, for if prepared in the latter way it is more apt to retain poisonous extractives; it is moreover not so digestible.

The necessary albumen may, therefore, be supplied chiefly from vegetables, eggs, milk and a sparing amount of meat. If meat is completely excluded from the diet, and I see no compelling

reason for doing this if the above restrictions are observed, care must be taken that a proper amount of albumen is given in the form of one of the other articles enumerated above; for unless the organism receives a definite amount of albumen (not less than 100 Grams in the twenty-four hours) it must consume its own tissues.

Milk is always a useful addition to the diet, for it is quite inoffensive, it supplies a certain amount of necessary albumen in place of the meat albumen and it seems to reduce intestinal putrefaction as manifested in a reduction of the urinary toxicity. I warn, however, against the exclusive milk diet that at one time was so fashionable as a panacea for all digestive, hepatic and renal disorders. The patients cannot tolerate it without serious detriment to their digestion, their cardiovascular apparatus and their general nutrition. It is to be considered a therapeutic measure rather than a dietary regrimen.

The sugars and starches of the food should be administered in abundant quantity in hepatic insufficiency; for in the first place, they are neither toxic in any way, nor do they lead to the formation of poisonous products in the bowels; in the second place, they must be considered distinct stimulants of the hepatic cells, so that they are useful when liver function is depressed; in the third place, they are highly nutritive and furnish much caloric energy; and, lastly, they increase the function of the eliminating organs. Too much of carbohydrate food is of course dangerous, for a starchy and sweet diet, as is well known, favors gastroenteric gaseous fermentation, meteorism, constipation and above all fatty infiltration of the liver.

To summarize, therefore, a case of hepatic insufficiency should receive a mixed diet, consisting largely of vegetables, bread stuffs, cereals, etc., with meat not more than once a day and selected, as to kind and preparation, as outlined above, with plenty of eggs and milk, with as little fat as possible, and with no spices, condiments or alcoholic beverages. That personal idiosyncrasies of taste and appetite, certain individual requirements, should be included in the calculation when selecting a diet for a sufferer from liver insufficiency need hardly be emphasized; that above all, especially in chronic cases, the patient should receive enough of each of the three essential food constituents, i. e., the albumens, carbohydrates and fats or fat-derivatives to insure adequate maintenance of the general nutrition need not be expressly mentioned, for, unless this rule is vigorously observed, all the manifold complications of underfeeding and malnutrition are bound to develop sooner

or later and the patient far from being benefited by the dietetic regulations and restrictions imposed upon him is literally slowly starved to death. Sometimes the task of striking the balance between the needs and the digestive powers is difficult.

2. A certain amount of putrefactive decomposition of the various food-stuffs always occurs in the bowel. This is manifested by the appearance in every normal urine of certain putrefaction alkaloids and of a variety of very complex organic compounds (conjugate sulphates, compound glycuronates, compound glycocolls, etc.) of which indican is the prototype, and by the excretion in the feces of various organic bodies that we know to be formed exclusively from the putrefaction of albumins. It is necessary to distinguish between the normal fermentative decomposition of the albumins, that is brought about by the action of the gastric and enteric secretions, and the putrefactive decomposition of these same albumins that is produced by many varieties of putrefactive microorganisms that gain an entrance into the bowel and there, unless checked in their activity or rapidly eliminated, exercise their pernicious effects. True, the decomposition of the albumins by digestive ferments and by putrefactive microbes proceeds along very similar lines and the end-products of either disassimilation of the albumin-molecule are highly toxic when introduced into the circulation, but there is just this difference between the two groups—the fermentation-splitting products are reconverted into serum-albumin in the bowel-wall, whereas the putrefactive end-products cannot undergo this reconversion and hence often pass unchanged into the blood and lymph-stream beyond.

Moreover, certain of the many putrefactive germs that occasionally lead a parasitic existence in the human bowel produce specific poisons of an albuminoid character that are frightfully toxic for the human species. Many of the latter have been isolated, and upon many of them a name has been bestowed. Others no man has ever seen but we know of them, to our sorrow, from their manifestations—from their physiologic effects. Among the symptoms that can be produced experimentally by various bodies that have been isolated from putrid bowel-contents are tetany and dyspeptic coma; some of the bodies produce violent headaches, others a feeling of general lassitude; some profuse outpouring of sweat, of saliva, of tears; others a suppression of these secretions, as manifested by dryness of the mouth and throat and skin; some dilate the pupils, others contract them; many of them produce skin-eruptions of the most varied kinds.

The character of all these symptoms and their intensity will depend upon the number and the variety of putrefactive bacteria in the bowel, upon the quality and the quantity of poison they secrete, upon the amount absorbed within a given time and upon the state of the resisting powers of the organism against the action of these toxins. In certain forms of intestinal putrefaction, e. g., the poison is so virulent and it is manufactured in such abundant quantities that most acute and alarming symptoms of diarrhea and profound general toxemia develop; in other forms, particularly in those that are accompanied or followed by constipation, the formation and absorption of the poisons is slower, and their character presumably also less virulent, so that we see develop a chronic form of autointoxication, manifested principally by headache, a coated tongue, loss of appetite, general lassitude, lack of ambition, chronic skin eruptions, itching, high arterial tension, dizziness and a depressed mood generally. The latter is the typical syndrome of the common form of intestinal autointoxication with hepatic insufficiency.

Recognizing this, the vital question is how to prevent this putrefactive decomposition of albumins in the bowel and thereby the formation and absorption of the poisonous products that can produce the above symptoms? As in any other form of treatment one cannot do better than to study Nature's way of combating the invasion of these parasites and the unfolding of their pernicious activity—and to imitate it and to reinforce it!

To the liver, chiefly, as we have shown in detail in previous paragraphs, is delegated this important function of restricting gastrointestinal putrefaction or of neutralizing its effects if it has once occurred. The liver fulfills this task in three different ways, viz.: (1) It pours into the uppermost portion of the small intestine a specific secretion that is capable, to a marked degree, of inhibiting the pullulation of putrefactive bacteria throughout the length of the whole intestine, and particularly in those first few feet where intact albumins should be disassimilated by the bowel ferments and not abnormally decomposed by parasitic microbes; (2) it attacks the bulk of any abnormal putrefactive decomposition-products of albumin that may, nevertheless, be formed and disintoxicates them so that they enter the circulation in an innocuous form and can be rapidly eliminated *via* the various emunctories of the body (chiefly the kidneys) without doing any harm, a process that is presumably brought about with the aid of a specific "internal" secretion of the liver cells (Massini); (3) it acts itself as an eliminating, i. e., an excreting organ in the sense that it pours back into the bowel, in

a non-toxic form, a variety of originally toxic bodies poured into the liver from the bowel; in this way the disintoxicated bowel poisons need not even travel through the whole cardiovascular apparatus before they leave the organism, but are returned, harmless, by the shortest route, whence they originally came from.

The bile, therefore, is both a secretion and an excretion. A "secretion" inasmuch as it contains a germicidal principle (and also, we must assume, that moiety of antitoxic "internal" secretion of the liver cells [see above] that is not utilized, i. e., combined with poisons within the liver); an "excretion" inasmuch as it contains a variety of disintoxicated poisons that the liver promptly returns to the natural cloaca of the body instead of the blood- or lymph-stream.

With the liver as an excretory organ we shall no longer have to deal in this article, for we are concerned principally in establishing what may be the character and the exact function of the liver-secretion that plays such an important rôle in the human economy. We shall have to see what this secretion is normally capable of accomplishing, what its active principle or principles may be, and shall determine what occurs when the outpouring of this secretion is arrested or when its character is perverted, and, finally, we shall point out and establish such means as are at our disposal for counteracting, on the one hand, the bad effects accruing from a lack of this secretion and, on the other, for stimulating the formation of an abundant quantity of this important principle when its formation is impeded or its normal character changed.

The bile is a mixture of the secretions of the liver-cells and of the mucous-cells lining the biliary passages and the gall-bladder. The mucus contained in the bile differs in no way from mucus secreted by any other mucous membrane and contains nothing that may be considered specific. The secretion of the liver-cells, on the other hand, contains several specific principles, i. e., ingredients that are not found in the secretion furnished by any other organ of the body. In addition the liver-secretion contains a variety of substances that are found in many other body-fluids, and that appear in the bile as *excretory* and not as *secretory* bodies; among the latter I need only mention urea, lecithin, cholesterin, ethereal sulphates, and a variety of mineral substances, as the chlorides and phosphates of calcium, magnesium and iron.

Neither the mucus of the bile nor the excretory substances voided in the bile interest us in this place, for we are chiefly concerned in determining which is the specific secretion of the liver

cells, the *active principle*, that can perform the many important functions that we have attributed to the liver, within the liver channels and, after it is voided, in the bowel.

The two most important of the specific elements of the bile are the *bile-acids* and the *bile-pigments*. The former appear in the form of the alkaline (potassium, sodium) salts of two bile-acids, viz., taurocholic and glycocholic, the latter in the form of a number of pigments that are all fundamentally related to a yellowish-green material called bilirubin and are known by the names of biliverdin, bilifuscin, biliprasin, bilihumin, etc.

Of these two groups of specific liver products the pigments must be considered to be excretory in character for they are physiologically inert, and they play no further role after they once enter the bowel; they are not reabsorbed into the blood or lymph from the bowel to exercise any effect in the tissues at large, but promptly leave the body in the stools after having undergone a variety of chemical modifications in the intestine that change their character considerably before they are ultimately deposited in the feces. There is even some doubt in regard to the claim that the bile-pigments are formed exclusively in the liver, for there is much experimental evidence to show that bile-pigments can be formed anywhere in the body where blood-pigment undergoes stagnation—witness, e. g., the yellowish-green discoloration of a bruise, of a hematoma, of sanguinolent exudates, etc. The pigments found in these foci cannot chemically be distinguished from the pigments found in the bile.

The bile-pigments, therefore, need not concern us further in our search for the active principle of bile (in the above sense). By exclusion, therefore, we are forced to assume that *the bile-acids are the only specific products of the liver-cells* that appear in the bile and that can exercise the important specific functions that this fluid can perform. This postulate is fully borne out by a mass of clinical and experimental data of which the following are the most important:

The bile-acids and their salts enter the uppermost portion of the small intestine in considerable quantities; an analysis of the stools shows that only a very small proportion reappears in the feces. Of about 4 Gm. of bile-acids, that a dog of 8 Kg. excretes in twenty-four hours, only about 0.5 Gm. appears in the feces (Bidder and Smith). The urine practically contains no bile-acids. Moreover bile-acids administered by the mouth reappear within a short time, not in the feces and not in the urine, but in the bile!

(Neisser, Experiments on Human Subjects with a Biliary Fistula). The lymph of the thoracic duct (Tappeiner) and the leucocytes of the circulating blood (Croftan) both contain bile-acids. From all these facts the conclusion is self-evident that the bile-acids are in great part reabsorbed from the bowel, perform an intermediary circulation from the bowel through the lymph- and blood-stream to the liver, and ultimately reappear in the bile—to be again poured into the bowel and again to travel the same circuit. This fact alone should teach us that *the bile-acids are an important and valuable principle that the organism does not waste but uses over and over again.* One is forced to the conclusion that these bile-acids must be intended to perform a variety of functions in various portions of the organism, viz., in the bowel, in the circulating blood and in the liver.

In the bowel, it has been known for a long time, that the bile-acids exercise chiefly four important functions, viz.:

1. They distinctly influence the peristalsis of the small intestine throughout its course. They act consequently as laxatives, by causing the rapid propulsion onward of the bowel-contents and by promoting that liquefaction of the solid and semi-solid albuminous ingredients of the upper bowel that alone can be brought about if an intimate mixture of the albumins with the enteric ferments and with certain bacteria is promoted.

2. They regulate the degree of fermentative splitting of the albumins and the carbohydrates. When this degradation occurs too rapidly much pabulum is wasted because it cannot be absorbed as rapidly as it is formed; hence the bile-acids, by checking, i. e., slowing this process when needed (and the outpouring of bile is reflexly regulated by the degree of disassimilation) promote better assimilation than if they were not present to inhibit enteric fermentation.

3. Their presence is absolutely necessary for the proper assimilation of the fats. Here they act physically by promoting the emulsification and saponification of fat-globules and by enabling the latter to adhere to the bowel wall and to enter the lacteal channels.

4. The bile-acids possess the power to a very marked degree of preventing the pullulation of many of the putrefactive bacteria that lead a parasitic existence in the bowel contents and that, if allowed to develop unchecked, cause abnormal putrefactive decomposition of albumin, with all the dire consequences that I have enumerated at length in previous paragraphs.

It will be seen, therefore, that the absence of bile-acids, a deficiency of this important liver-secretion, can produce serious perversions in the bowel in four different directions, viz.: (1) By depriving the bowel-wall of an important stimulus to peristaltic movements they cause stagnation of bowel-contents and incomplete mixture of undigested material with digestive ferments; (2) by allowing the degradation of albumin and carbohydrates to proceed unchecked they cause too rapid disassimilation of these bodies with inadequate absorption; (3) by preventing the proper emulsification and saponification of the fats they prevent the assimilation of this important food and deprive the organism of this pabulum; (4) by allowing intestinal putrefaction to go on unchecked they favor abnormal degradation of albumins, loss of nitrogenous material and *general autointoxication with resulting cardiovascular, nervous, hepatic and renal disorders.*

In the *blood* the bile-acids perform equally important functions.

I have shown that the bile-acids perform what may be called an *intermediary circulation* from the bowel back to the bowel, traveling through the blood and lymph-stream to the liver and thence in the bile to the intestine. This fact was deduced from four observations, viz.: (1) that only a fraction of the bile-acids that are poured from the liver appear in stools; (2) that bile-acids given by mouth reappear in the bile (as observed in animals and human subjects with biliary fistulæ); (3) that the lymph of the thoracic duct always contains bile-acids; (4) that the leucocytes of the blood also carry bile-acids.

From this observation comes the self-evident conclusion that the bile-acids are not an excretory product but a *secretion* of the liver that is so valuable that it is used over and over again. That the bile-acids perform a variety of important functions in the bowel was set forth in a preceding paragraph; it remains to be shown what functions the bile-acids can perform while *en route* from the bowel *via* the blood and lymph-stream to the biliary channels of the liver.

From toxicological studies we know that bile-acids or their salts can exercise the following nine effects upon the blood, the cardiovascular apparatus and the nervous centers (quoted from Croftan.—*Am. Journal of Medical Sciences*, Jan., 1902).

1. They have a powerful cytolytic action. Injected even in small doses they produce a wide-spread disintegration of the red blood-corpuscles, with a liberation of their hemoglobin; brought in contact with other cells of the body they cause their disintegration.

2. They have a distinct cholagogue action—are, in fact, the only substances known to possess this power, and actually cause an increased flow of bile.

3. They aid coagulation in small doses (1 : 500).

4. They stop coagulation in large doses (1 : 250 and over).

5. They slow the heart-beat by a direct action on the heart-muscle and the cardiac ganglia.

6. They act as vasodilators in very small doses.

7. They act as vasoconstrictors in large doses.

8. They reduce motor and sensory irritability.

9. They act on the higher cerebral centers, causing coma and stupor.

Many of these effects, it must be remembered, however, are only produced when the bile-acids or their salts are forced into the circulation in large doses by direct intravenous injection. Normally only very minute quantities of these bodies are found circulating, so minute, in fact, that for many years after the intermediary circulation of the bile-acids was postulated *a priori*, chemists failed to actually demonstrate their presence in the blood. The reason for this was made apparent by Croftan (l. c.) who showed that the bile-acids never occur free in the serum, but are always carried by the leucocytes (white cells) of the blood. The latter harbor these substances in a harmless form and carry them safely through the blood-stream, liberating only so much of the bile-acids at a time as is needed to produce the effect that they are capable of exercising.

In the small doses, then, in which bile-acids are normally liberated in the blood-stream they can only exercise effects 1, 2, 3 and 6 of the above series, viz., they aid in the normal destruction of blood cells, chiefly red blood-corpuscles; they act as a distinct stimulant to the flow of bile; they aid in the coagulation of the blood; they play an important role in the mechanism of vasoconstriction and vasodilation.

Inversely, deficiency of bile-acids from the bowel, and hence from the circulating blood, must seriously interfere with the normal exercise of these four functions. In the first place dead blood-corpuscles (chiefly red ones, carrying hemoglobin that clamors for liberation) undergo slower disintegration than normally so that the spleen and the finer capillaries become choked and occluded; this leads to a variety of disturbances that are self-evident; also to changes in the character of the bile-pigments and hence of the physical constitution of the bile; for the formation of normal bile pig-

ments is dependent on the liberation and proper disintegration of the hemoglobin that is freed from dead red blood-corpuscles.

The result of these changes in the bile is viscidity of the contents of the bile-channels and gall-bladder, stagnation and backing-up of bile, and hepatic insufficiency. Here, then, is a vicious circle, viz.: The insufficiency of the liver-cells (due to any one of the many causes I have enumerated) causes a deficiency of bile-acids in the bowel and hence in the blood, this interferes with the normal disintegration of red cells and the liberation of hemoglobin; and as a result of all this we witness changes in the bile, stasis in the bile channels, pressure on the liver-cells and consequently further interference with their function—hepatic insufficiency. How important it is in such cases to supply the bile-acids by mouth, that the liver is unable to properly secrete!

In the second place absence of bile-acids from the bowel, and hence from the blood, deprives the liver, as I have stated, of the most efficient, possibly the only *real* cholagogue that we possess. It appears that the bile-acids are the chief physiological stimulant of the liver cells—in certain directions. While there is no evidence to show that the administration of bile-acids stimulates the urea- or uric-acid forming function or the glycogenic function (i. e., the function of the liver to convert sugars into starch glycogen and to store it as such for future use), there is abundant evidence to prove that the bile-acids are capable of stimulating a colossal flow of bile and, by implication, of bile-pigments and bile-acids.

What a wonderful and highly effective process this is, that the product of a cell can stimulate the same cell to manufacture more. We have in this intermediary circulation of the bile-acids a self-regulating mechanism that responds automatically to the varying calls of supply and demand, that reduces the production of a most valuable secretion to the lowest efficient minimum and wastes nothing. We have many analogous processes in the body.

Again, we see, that the supplying of bile-acids, should they become insufficient to stimulate their own formation, is a therapeutic procedure of the greatest value and one that is altogether rational; and we also see that unless this step is taken, a second vicious circle, similar to the one described above, is created, in the sense, namely, that deficiency of bile-acids again changes the character of the bile, from lack of cholagogue stimulation, causes viscidity of the bile stasis of its current, throught the bile ducts compression of liver cells and further interference with their functions, in other words, hepatic insufficiency.

Lastly we see that absence of circulating bile-acids profoundly disturbs the finer mechanism of vasoconstriction and vasodilatation. When we consider that the blood-pressure is directly dependent upon the caliber of the peripheral arterioles and capillaries, it is clear that interference with the normal changes of the lumen of these vessels must exercise a profound influence upon the heart and the whole arterial tree. What that means is self-evident, viz., nutritional disorders throughout the body as a result of abnormal blood supply; this disturbance first becoming manifest in the nervous centers that are so susceptible to even slight alterations in their blood supply, later appearing in other organs.

If the disturbance lasts for long periods of time the inevitable result is arteriosclerosis, cardiac hypertrophy and myocarditis and all the evidence of chronic malnutrition, appearing first, naturally, in those organs that are supplied by *end arteries*, viz.: the brain, the kidneys and the retina. Cardiovascular changes with cerebral, retinal and renal changes spell *Bright's disease*, interference with general nutrition means suboxidation, metabolic disorders, viz.: *diabetes*, *obesity* and all the protean manifestations of the socalled *uric-acid diathesis*.

The absence, therefore, or chronic deficiency, of bile acids from the bowel and hence from the circulating blood is due to hepatic insufficiency. The causes that produce the latter state can, to a great extent, be removed by preventing intestinal putrefaction—and for this the sovereign remedy, as we have shown at length, is the bile acids.

The relief of hepatic insufficiency is further promoted by the exhibition of bile acids, inasmuch as the latter aid materially in stimulating the liver cells to increased bile-formation and in carrying to them the material they require to manufacture bile in the form of free hemoglobin.

Symptomatically, the administration of bile-acids is indicated as a *substitution therapy* because many of the signs of hepatic insufficiency are caused by absence of the bile-acids from the blood.

Finally, in very many maladies that begin with slight nutritional disorders and increased arterial tension, due, in many instances, to bowel putrefaction and hepatic insufficiency, the bile acids are a valuable remedy—and this applies, as I have shown, to a large variety of chronic disorders of which arteriosclerosis, diabetes and Bright's disease are important prototypes.

The bile-acids, therefore, that in a circumscribed sense may be considered *the active principle of the bile*, should be employed in

a host of conditions that have been described above. They are by no means a panacea for all ills, but I consider them, when judiciously exhibited and when administered according to the indications that I have been at some pains to clearly formulate in this article, to be predestined to recognition as one of the most valuable latter-day adjuvants to our therapeutic armamentarium.

BOLDINE

Standard granule—gr. 1-67, Gm. .001.

From Peumus boldo are derived an alkaloid, boldine, and a glucoside, boldo-glucin. Boldine increases the elimination of urea and the secretion of bile. Taken by the stomach it causes a bitter taste (being evidently partly eliminated by the saliva) and a sense of heat in the stomach. It increases the appetite and the digestion as well, displaying specific action upon the liver. Chronic hepatitis, jaundice, hypertrophy of the liver, hepatic colic and hepatic maladies contracted in the tropics, have been successfully treated by boldine. Bilious vomiting, headache and jaundice disappear under its use.

Houdé recommends boldine highly as a remedy for gallstones. Naunyn says that these are formed not only in the gall-bladder but in the biliary ducts. Cholesterin and calcium bilirubinate, the principal chemical components of biliary calculi, come from the mucous lining of the biliary passages. The lithogenic mucous catarrhs may be provoked by microbes (bacillus coli, Eberth's bacillus, etc), and are therefore of infectious origin. Such catarrhs are not acute, but the product of microbes whose virulence has become much attenuated. They cause stagnation of the bile in the ducts, though not a total obstruction, the bile being evacuated normally. Normal bile is scarcely sterile, the colon bacillus being only sparsely found in this fluid. The cause of concretions is found in the retarded flow.

Some calculi form rapidly, others more slowly. They may remain a long time in the gall-bladder without giving rise to any symptoms whatever. They do harm by exciting catarrh, cholecystitis and cholangeitis. If of infectious origin the bacilli multiply rapidly. The calculi interfere with complete evacuation of the bile, with results similar to those due to the retention of residual urine in the urinary bladder, as the residual bile forms an excellent medium for the cultivation of infectious bacteria. Thus, a nidus may be formed for grave autointoxications, or infections of the bowels, the colon bacillus becoming very virulent in residual bile.

The resultant cholecystitis may provoke the expulsion of the calculi, producing the agonies of hepatic colic with subsequent jaundice; or the attack of colic may itself cause the cystic inflammation.

Recovery may ensue in every stage of cholelithiasis if all the concretions are evacuated, by the gall-passages or through fistulous tracks. By a "cure" is meant the cure of the infectious affection; when the lithiasis becomes latent, the ducts being pervious. This cure may be permanent or only temporary. The most approved method of cure is the production of an abundance of bile. It does not follow that an agent that will produce this in health will do so when the biliary passages are obstructed. Cholagogs lose their efficacy in the presence of infectious cholangeitis.

So much for Naunyn, whose skepticism as to efficacious treatment is simply the expression of modern European therapeutic nihilism.

Houdé places boldine in the front rank of remedies for cholelithiasis, for its cholagog action is rarely wanting.

Dujardin-Beaumetz and Bourgoin found that it notably increased urea elimination, and especially the bile excretion, without affecting the circulation, the temperature, or the quantity of the urine. This gives to boldine the character of a true hepatic stimulant. The first notable effect is an increase of the bile, then follows a diminution of hepatic congestion. When appendicitis depends on defective bile-supply it is favorably influenced by boldine, which sweeps out all organic residues whose stagnation sets up this affection. Boldine should also prove effective in the hepatic maladies consequent on prolonged residence in tropical countries. In malarial hepatitis boldine has not proved efficient, unless quinine is administered at the same time. Sodium arsenate renders the combination still more effective.

In Parke, Davis & Co.'s Pharmacology of the Newer Materia Medica, boldo is pronounced by Zaremba most useful in gonorrhea, in atonic dyspepsia with or without biliousness, in chronic cystitis, in chronic hepatic abscess, and as a powerful anthelmintic. Eliminated through the urine, boldine increases the excretion of urea but not of water. The glucoside, boldo-glucin, has marked hypnotic properties, and is also said to compare favorably with cocaine as a local anesthetic.

Merck's Index gives the dose of boldine as gr. 1-10 to 1-30.

Houdé advises boldine in granules of Gram 0.001 (gr. 1-67), each, of which six to twelve should be given daily. I have pre-

scribed five to ten of these granules together at bedtime, with very good results. In one case where the renal elimination had fallen to 20 oz. daily, containing 350 grains of solid matter, five granules at bedtime raised the elimination to about 600 grains and the quantity to 64 oz. In another case, the elimination of solids rose from 300 grains to 600 and 800, with corresponding improvement in the symptoms and feelings. Two cases are of course too few for positive conclusions, but the results in these warrant me in advising a trial of boldine in these cases of defective elimination which have proved so intractable to treatment.

Houdé says that "boldine does not influence the circulation, temperature, or the quantity of urine, but augments sensibly the elimination of urea and the secretion of bile.

"Laborde found boldo exercising primitively a hypnotic action on the nervous system, with temporary suspension of the functional acts of conscious life and of relation. This was accompanied by a certain degree of anesthesia, general and of special senses, notably of hearing, and abolition of the oculopalpebral reflex. After morphine, codeine, narceine and hyoscyamine, boldine ranks with the secondary hypnotics; but its action on the liver makes it precious in cases where the other hypnotics are objectionable. Here boldine relieves pain and favors evacuation, as in biliary calculi and other forms of calculi and obstruction.

"This observation of Laborde harmonizes with our own. Of all the hypnotics we have tried, but one resembles boldine—narceine. The sleep induced by the latter leaves a certain degree of consciousness, which boldine does not, but the awakening is as free from disagreeable sensation in the one case as in the other. Narceine, like all opium derivatives, cannot be administered during digestion, at least during the first part, which is not the case with boldine.

"Boldine causes considerable increase of the biliary secretion, and dissipates hepatic congestion and functional ailments of this organ. In simple jaundice, hepatic colic, chronic hepatitis, appendicitis, and hepatic ailments of hot or unhealthy countries, the good effects of boldine are no less manifest. It is in fact a specific for hepatic maladies in general, even for cirrhosis.

"Boldine does away with the failures encountered in using boldo; due to manifest insufficiency of the dose. Of the granules containing each Gram 0.001 (gr. 1-67), the daily dose is 6 to 10, which are always efficacious in acute hepatic colic, biliary calculi and acholic jaundice. One kilogram of boldo contains Gram 0.02

to 0.03 of pure boldine, so that the effects of the ordinary medicinal doses of the crude drug are insignificant.

"Boldine favorably influences appendicitis, which ends without suppuration. The abundant production of bile induces a general evacuation of all the organic residues in the bowel, whose stagnation is the point of departure of inflammation of that part of the intestinal canal.

"Boldine ameliorates alike the hepatic affections due to any form of alcohol, to a diathesis, or to a residence in hot or unhealthy countries. Hypertrophies of paludal origin feel its good effects as well, but the improvement is more rapid if quinine is also given. With profound debility, sodium arsenate should be added. Begin with one granule Gram 0.001 five times daily, gradually increasing until the daily dose reaches ten granules, if necessary and well supported. But if the hypnotic effect is desired give a granule every fifteen minutes at bedtime. Six granules secure six to eight hours' normal sleep."

BRUCINE

Standard granule—gr. 1-134, Gm. .0005.

Brucine is the companion alkaloid of strychnine in nux vomica and ignatia. Brucine exists in nux vomica seeds in the proportion of 1-2 to 1 percent, strychnine being present in from 1-4 to 3-5 percent.

Brucine is soluble in 320 parts of cold and in 150 parts of boiling water; very soluble in dilute or in absolute alcohol, in chloroform or in benzole, very slightly in benzine, not at all in ether. The salts are freely soluble. Brucine is even more bitter than strychnine.

Physiologic Action.—There is much diversity in the reports on the action of brucine, partly due to the difficulty experienced in obtaining it free from strychnine. Reichert said it was precisely similar in effects to strychnine, except that the latter is more quickly absorbed, and exerts forty times greater convulsant force; brucine having greater toxicity as to the sensory nerves. Cushny also states that brucine exerts much more action on the nerve-ends in voluntary muscle than strychnine. But Wintzenried says brucine stimulates the spinal cord, paralyzes the motor nerves and has no effect on the cerebrum or the sensory nerves; at first raising and then depressing arterial pressure; while large doses paralyze the vagi, death occurring from asphyxia. When taken by the mouth

no symptoms ensue, because the drug is excreted as fast as it is absorbed.

Reichert says it causes a brief motor paralysis before the convulsions; but Shoemaker affirms that it may cause death without any convulsions.

Brunton states that brucine checks oxidation of the blood and the excretion of carbonic acid; greatly increases reflex excitability; causes tetanic convulsions; and acts as a stimulant to the respiratory center, making the respirations deeper and quicker, and the lungs do more work.

Although brucine requires a longer time for absorption than does strychnine, death comes sooner when lethal doses are given, because the former is quicker in getting to work. We cannot therefore subscribe to the view of Murrell, that brucine is only a mild strychnine and completely represented by the latter in small doses. We have repeatedly noted the quickness with which the effects of brucine are manifested, and in many cases this is of the utmost value, as time may not be allowed for the slower remedy.

Therapeutics.—In many emergencies the speedy action of brucine renders it preferable to strychnine. By its quick action and rapid elimination, brucine is admirably adapted to the intensive dosage, the use of small and oft-repeated doses. While it is said to have only one-fortieth the strength of strychnine, we rarely find it advisable to give more than gr. 1-67 to 1-134 of brucine, repeated every five to thirty minutes till the requisite degree of tonicity is attained. When it is desired to keep up this effect, strychnine may be given with or after brucine. In emergencies when quick action is eminently or urgently indicated, from gr. 1-12 to 1-2 may be given at once; but personally the writer has never found it necessary to exceed gr. 1-8. In one case of alarming heart-failure from overexertion, in a man aged over seventy, this dose was given, with atropine, gr. 1-134, with the best effect, and permanent recovery ensued. This case had been diagnosed as a "hopeless" case of heart-clot by a distinguished practician and teacher, and left with that prognosis.

When the salts are employed, and administered in solution, in hot water or hypodermically, the effects of brucine are most valuable in syncope, from sudden loss of blood, exhaustion from heat and excessive water-drinking, or from the effects of depressing drugs or exhausting discharges.

Merck advises his brucine in doses of gr. 1-12 to 1-2; maximum single dose gr. 3-4, daily, maximum dose 3 grains.

Mays reported that brucine exerts a marked local anesthetic effect, in solutions of 5 to 10 percent. This has been confirmed by Seiss, who pronounces it less reliable than cocaine, and found large doses cause nervous irritability lasting several hours. The writer has employed a mixture of brucine and cocaine, 2 to 5 percent of each, in some cases in which the latter alone gave rise to symptoms of collapse, with excellent effect.

Burnett tried brucine locally in pruritus, etc., and preferred it to cocaine. In chronic forms of pruritus it is effective, and preferable to cocaine as not being liable to result in an injurious habit. In fact, this local anesthetic effect of brucine may indicate its value as a substitute for morphine and cocaine when these are used hypodermically.

In making solutions of brucine salts Wood advises the addition of one drop of sulphuric or hydrochloric acid for each three grains of the drug.

The antidotes to brucine are chloral, chloroform and tannic acid.

The seeds of nux vomica contain about 2.88 per cent of alkaloid, equally divided between strychnine and brucine; Strychnos tieuté contains 1.429 per cent of strychnine and traces only of brucine; Strychnos ignatia has 1.39 per cent strychnine and traces of brucine; the bark of false angostura and that of Strychnos colubrina contain about 2.4 percent of brucine and traces of strychnine; Strychnos ligustrina has brucine alone; and Strychnos gautheriana —Hoangnan—contains traces of strychnine and 2.7 percent of brucine. These are but averages, the true composition of each differing in various samples; so that the use of the galenic preparations of these potent plants gives a variety and uncertainty the reverse of pleasing. Falck examined some specimens of nux and found the tincture containing from 0.244 to 0.353 percent, the alcoholic extract from 7.3 to 8.59 percent, equally divided between strychnine and brucine; while the aqueous extract contained 3.18 to 4.3 percent, one-fifth strychnine and four-fifths brucine.

Brucine is for children and persons in feeble health what strychnine is for adults and persons strongly constituted. For the child brucine is the incitant *par excellence*. Brucine may be given to infants a granule at a time, every quarter hour in acute cases, till effect; four to six granules a day in chronic affections, with other remedies as indicated. For adults very susceptible to strychnine two to four granules may be given at each dose (Van Renterghem).

Bouchardat denied that there was so great a difference between brucine and strychnine as is usually claimed, and Laura agrees with him. The Italian clinician employs brucine for children and delicate adults to replace strychnine. He especially advises brucine for gastric and intestinal muscular atony, with tympanites, interfering with peristalsis and altering the secretory function of the innumerable glands of this tract, preventing the regular, complete and rapid digestion of food, interfering with nutrition and inducing diarrhea, constipation or an alternation of the two. This is a frequent condition with children and entails perils. In infantile paralyses also he has employed brucine with success, adding significantly: "The cures obtained with the poor infants of our children's hospital are no secret either for the physicians or the benefactors of that institution." He agrees with Burggraeve that brucine aids the generative function without causing collapse or syncope as do the aphrodisiacs. "Experience has demonstrated that it is wise to guard carefully the secret of the most vaunted aphrodisiacs, the source of the gravest accidents and even of death." The knowledge of such remedies is emphatically a professional secret, which we have no right to share with the laity, who have not the ability to utilize it but are likely to do themselves and others irreparable injury by a misuse of these powerful remedies.

Laura places the dosage of brucine "a little higher than that of strychnine," and adds that no harm can be done by administering minute doses in rapid succession until the desired effect has been secured. If the case demands prolonged treatment with brucine this should be suspended from time to time, or the doses sensibly diminished to allow the system to recover its susceptibility. After four or five days' use, omit the remedy for one or two days. During these intervals the body should be abandoned to the great hygienic modifiers.

BRYONIN

Standard granule—gr. 1-67, Gm. .001.

From Bryonia dioica is derived the glucoside bryonin. It is colorless, very bitter, soluble in water and in alcohol, insoluble in ether or in chloroform.

Large doses of bryonin cause grave inflammation of the stomach and bowels, vomiting, uncontrollable diarrhea, vertigo, fall of heat, dilation of the pupils, cold sweating, colic, collapse, extremely small pulse, and death (Felter-Lloyd). Bryonin is less irritant

than the galenic preparations and in moderate doses is simply laxative.

Therapeutics.—Bryonin has been recommended for convulsions due to intestinal worms, for dropsy, chronic inflammations with enlarged glands or serous effusions; in scarlet fever to prevent ear complications; chronic orchitis, rheumatism, pleurisy, pulmonic disorders, fevers, to relieve constipation (Felter-Lloyd).

The authors just quoted enumerate its indications as follows: In lung diseases, for sharp, cutting, lancinating pain with harsh cough; pain intense and tearing, worse on motion, parts feel stiff, sore and bruised, much mucus in bronchioles; pulse hard, frequent and vibratile, high fever; right cheek flushed; for serous inflammations, peritonitis, or synovitis; frees circulation, overcomes capillary obstruction, lowers fever and controls pain; lessens nervous excitation and erethism, and promotes secretion and excretion; for rheumatic conditions of the chest and pleurodynia; best in pleurisy, especially if insidious and complicated, when bryonia stimulates absorption; bilious pleurisy, pleuropneumonia, bronchitis with blood-streaked sputa, pneumonia with pleuritic pain or short, sharp cough, worse on motion; in typhoid pneumonia, with baptisia; in phthisis to control pain, fever and cough; for cough and pain in influenza it excels all other remedies but gelsemium; for laryngeal and tracheal cough, dry, rasping, hacking and explosive, with tensive, sharp pains, little secretion; irritative cough aggravated by talking, eating, or entering a warm room; the condition is a debility and patients sweat easily; it often controls fever when ordinary remedies fail; chilliness, tension and easy sweating indicate bryonin; with peculiar pains, deepened color of mucosa and full veins, frontal headache, dry tongue and tendency to delirium.

Bryonin is excellent in hepatic disorders with jaundice, high-colored urine and pain on pressure, stitching, sticking or cutting pains about liver; acute or chronic rheumatism; painful and stiff spine in children, rheumatic headache, sharp temporal or frontal pain, tender scalp, worse on motion; rheumatism of fingers (Locke); ovarian and menstrual wrongs with tenderness; acute mammitis; partial deafness from cold or scarlet fever; scrofulous eyes, ears, ulcers and synovitis, with stinging, burning pains; tensive earache in children; facial neuralgia with weak heart, cold hands and feet; rheumatic iritis with pain on moving eyeball; heart-strain and organic heart troubles when exposure and rheumatic twinges bring on the paroxysms; peritonitis with colicky pain, unusual tenderness and tension; pericarditis tending to hydropericardium; brain dis-

orders with serous exudation; indigestion, food lying heavy like a stone; typhoid fever with pulmonary complications; abdominal tenderness and pain in typhomalaria, zymotic diseases; and in cholera infantum where it should be given with ipecac or euphorbia (Scudder).

Scudder gives the specific indications for bryonia as: A hard vibratile pulse, flushed right cheek, frontal pain extending to basilar region, and irritative cough.

Felter and Lloyd insist on the pain worse on motion as a cardinal characteristic.

Ellingwood says this remedy acts along three lines; first, specifically upon serous inflammation; second, upon inflammation of the synovial membranes; third, on acute inflammatory conditions with tenderness on deep pressure, or quick, sharp, shooting pains. It is certainly a remedy for acute pain in inflammatory disease, with the pain aggravated by movement or relieved by pressure; when there is fever with hard, frequent, vibratile pulse, the muscles sore and tender, as if bruised, the cheeks flushed, or when from fever there is frontal headache extending to the basilar region.

We have given the eclectic accounts of this drug in full because it is one they value very highly. In the writings of the regular school but little is to be found on this once popular remedy. Van Renterghem tried bryonin on his own person, taking gr. 1-12 every hour till gr. 1-2 had been taken. No abdominal pain ensued, nor action on the bowels, the night was passed in comfort and at 6 a. m. he was awakened by the calls of the bowels, passing semi-solid stools. The action followed in eight to twelve hours. Doses of gr. 1-2 to 1 1-2 purge violently with atrocious pains and choleraic sy mptoms. As synergists he enumerates jalapin, colocynthin and elaterin; with podophyllin in large doses. Atropine is an excellent auxiliary and corrigent, by its antispasmodic power and as a regulator of peristalsis. Morphine, cotoin and tannic acid antagonize bryonin. He suggests its use as a succedaneum for podophyllin. Acting specially on the cecum, bryonin relieves this and the colon from torpor. The field for it is in abdominal torpor, bilious fevers and dysenteries, verminous and stercoral colics. To him it is evidently a cathartic and no more.

Laura calls attention to the violent effects following overdoses of bryonin, such as sharp intestinal pains, depression of the bodily forces, and, if the dose is large enough, even death. In the doses employed by modern therapy bryonin is a tonic and an incitant of the gastric functions, useful in atonic and flatulent dyspepsias with con-

stipation, but without inflammation or active irritation of the intestinal apparatus. It exerts a selective influence over the rectum. He questions its asserted control over syphilis and scrofula.

Burggraeve says it is a remedy little used but capable of relieving the large intestine of its torpor, acting specially on the cecum and thus terminating the digestion favorably; useful in hypochondria, especially for the attendant constipation; it may be given with jalapin an hour before meals. He gave six to eight granules daily, each containing a milligram—gr. 1-67.

Shaller found that bryonin stimulated the kidneys, increasing the quantity of urine. He recommends it in all forms of dropsy, to promote absorption of the effused liquid. For torpid liver and biliousness he finds it of value. In serous inflammations, after fever has been reduced by aconitine, there frequently remain various painful and annoying conditions that may last years; such as the headaches after meningitis, the stitch in the side after pleurisy, the precordial pain of chronic pericarditis and the joint ails after rheumatism—all which are cured by bryonin. The principal field for bryonin is in the alleviation and cure of chronic inflammations of serous membranes. He advises doses of gr. 2-67 every two hours till decided physiologic action is denoted by thorough evacuation of the bowels; then half this dose. If pain ensues he adds atropine. Several weeks are required to cure chronic affections.

Dr. W. B. Robertson found that a few granules relieved the stiffness following long bicycle rides by a novice.

Dr. C. Stanton gave gr. 1-67 every fifteen minutes for neuralgic headache and got relief from the second dose. To a lady who had stopped menstruating for two months from cold he gave gelsemin gr. 1-134 and bryonin gr. 1-67 every half-hour till the menstrual discharge appeared, which was less than twenty hours.

Dr. W. H. Blythe reports the case of a man who had been injured in the chest by the handles of a truck. He could not turn over for pain. He was given bryonin gr. 1-67 every two hours, and after taking 17 doses was able to leave his bed.

BUTYL CHLORAL HYDRATE

Standard granule—gr. 1-6, Gm. .01.

Butyl chloral hydrate, formerly known as croton chloral, is a remedy with but one clear cut and distinct indication. It was introduced by Liebreich as a remedy for painful affections of the trigeminal nerve. This property is denied by von Mering, who, with

Cushny and Wood, consider it does not materially differ in action from the ordinary chloral hydrate. But Hare states that it is more analgesic and less depressant to the heart and circulation, and better for insomnia due to pain. It is quite effective in facial neuralgias and migraines, especially if the fifth nerve is affected; also for headaches due to eyestrain, sick headaches not dependent on disorder of the stomach or on nervous debility; and while useless in toothache is beneficial in neuralgias dependent on decaying teeth—a very nice point in diagnosis!

Liebreich found that toxic doses caused deep sleep, trigeminal anesthesia and stopped the respiration, the circulation continuing. Von Mering found it lessened the blood-pressure.

Butyl chloral relieves the pangs of tic douloureux with striking quickness. The dose required to relieve pain is smaller than that necessary to produce sleep. The sleep is short as compared with that due to chloral hydrate. Complete trigeminal anesthesia requires doses of thirty to sixty grains; by which the corneal reflex is abolished, and yet the spinal cord is unaffected, as the reflexes of the trunk and extremities and the muscular tonicity are normal, as well as the pulse and respiration.

Bronchial irritability is relieved by butyl chloral, and Shoemaker speaks of it as assuaging the pains of dysmenorrhea.

Dentists administer this agent to allay the suffering from inflammation of the pulp or the peridental membrane, or the pain of a recent filling that is making itself disliked. Mixed with equal parts of menthol and carbolic acid, it is applied on cotton to carious cavities, the mouth in all cases being washed first with sodium carbonate solution.

Butyl chloral is but slightly soluble, in cold water 100 parts, in 4 of glycerin, freely in alcohol, ether or hot water.

For over-doses the antidote is strychnine in doses sufficient to excite the spinal cord. *Per contra*, butyl chloral is an efficient antidote in strychnine poisoning.

The dose as an analgesic is usually given as gr. iij to v, every two hours; as a hypnotic gr. xv to xx; but excellent results are obtained from a grain every quarter-hour. The powder is irritant to the stomach. Brunton recommended administration in syrup of tolu or in almond mixture. Another mixture is butyl chloral 5 to 10 parts, glycerin and alcohol each 20 parts, distilled water 100 parts.

This is a safe and effective anodyne and hypnotic for little children, who can take a granule containing gr. 1-6 repeated at very short intervals. It is somewhat difficult to distinguish the

varieties of headache that are amenable to butyl chloral, but in general those due to eye-strain and where the pain seems to be confined to the scalp, are relieved by this agent with remarkable quickness.

Von Mering's conclusions were derived from experiments upon animals in a state of health; and, as Binz remarks, these negative results prove absolutely nothing against the positive ones obtained by clinical trials with human beings when ill.

Yeo administered butyl chloral with success in nervous and spasmodic coughs, and Nicholson found it effective against whooping-cough.

Butyl chloral has been used with advantage to anesthetize the eye or the face before operations on these regions.

Van Renterghem gives ten granules repeated every ten minutes for tic douloureux; for insomnia triple this dose, continued till effect. He has succeeded in relieving tooth-ache by introducing a granule in the cavity of the aching tooth, repeating two or three times.

CACTIN

Standard granule—gr. 1-67, one milligram; gr. 1-134, one-half milligram.

Cactin is a concentration from the blossoms and young, tender stems of cactus grandiflorus, a plant indigenous to Mexico and the West Indies, where it was at one time a popular remedy for various diseases, such as irritation of the kidneys and bladder, intermittent fever, difficulty in breathing, cough, etc.

Cactus grandiflorus, or cereus grandiflorus, most familiar under the name of night-blooming cereus, is a green-stemmed climber, very sensitive to frosts, but frequently cultivated in temperate regions where its magnificent flower, from eight to ten inches in diameter, opening after sundown, and decaying next morning, is an object of interest and delight.

Both the young and the tender stems of the plant, and the flower, are used in medicine, the flowers being tinctured immediately on opening, the stem being worked fresh.

Much needless confusion has existed among collectors of the drug, and many different species and varieties of cactus have been inexcusably substituted for it in medicine. Unfortunately, all these sophistications are practically worthless, and their frequent substitution for true cactus grandiflorus may account in a measure for the contradictory reports that are prevalent in medical literature upon the merit of the drug.

Lloyd Brothers, in Cincinnati, Ohio, say that they prefer to use for their preparations the open air plant collected in a sun heated part of the tropics, where frost does not occur, rather than that raised in the greenhouse, and they believe that the long and extensive use of their preparations by physicians fortifies their conclusion, which is based on much experience concerning the quality of the tropical grown open air plant.

We are informed in Lloyd's Drug Treatise II, 1903, that Cactus Grandiflorus is mucilaginous, and yields a sticky juice. The green stems form a viscid pulp when pounded in a mortar. Its qualities are of a resinous nature, and are abstracted by alcohol. No water is admissible. Its active constituents have not been determined other than that they are related to the resinous substance. The inorganic constituent is oxalate of calcium and the acid is tartaric acid (Kunzé).

According to Merck, its constituents are: Cactine; acrid resinous glucoside; resins; fat; wax, etc.

"Differentiating chemical tests are altogether wanting for the constituents of cactus grandiflorus, so that at present no possible method of chemical or physical investigation can determine the authenticity of a preparation of true cactus grandiflorus, or distinguish it from that of an imitation made of any one of the hundreds of other common and usually cheaper species and varieties of cactus. For this reason physicians must rely altogether on the intelligence, care and integrity of the manufacturer whose preparations they use and whose record is established in medicine. Our experience has been that for months together we could supply no cactus grandiflorus under our label owing to the difficulty in obtaining the genuine crude drug in prime condition, although substitute species were available by the ton at comparatively little cost." (Lloyd's Drug Treatise II, 1903).

As already indicated, Cactus Grandiflorus is said to be used by the natives of its habitat (Jamaica) for fevers, difficulty of breathing and many other affections. It is also employed in Mexico for like purposes. Possibly its reputed virtues in the direction of the respiratory organs led to its consideration as a heart remedy, the first record of its use being by the German Dr. Scheele, whose research, however, passed practically unnoticed until Dr. R. Rubini, a homeopathic physician of Naples, brought the drug into conspicuity as a heart remedy. Cactus Grandiflorus or "Cactus" is thus a remedial agent of homeopathic introduction, in which school it was exclusively employed for many years. When Dr. J. M.

Scudder issued "Specific Medication," 1870, he accorded to cactus an important place. Under his favor its reputation extended so that all eclectic authorities became familiar with its virtues and commended it without reserve. The most comprehensive and complete early study of the cacti family in medicine is that of Dr. Richard E. Kunzé in the Transactions of the New York Eclectic Medical Society, 1875 and 1876. Innumerable journal contributions as well as all the books on materia medica issued in the eclectic school have contributed to the praise of cactus. Indeed, it is evident that in America credit for the bulk of cactus now used outside homeopathy is due either to the influence of eclectics direct or to their professional affiliations (Lloyd).

While we thus owe the knowledge of the drug to the homeopathic and eclectic schools, the therapeutic uses of cactus grandiflorus and its preparations are as firmly determined and established among clinicians of the old school as they are disputed and denied by laboratory workers and scientists. Especially has the plant and its position in the materia medica as a cardiac remedy been fiercely assailed in the last few years, several laboratory workers who had no clinical experience whatever, having determined on frogs and small mammals entirely to their own satisfaction if not to that of the general practician, that the plant and the preparations made from it were entirely inert and of no practical value whatever. Particular stress was laid upon the fact that cactus and cactin do not exert a digitalis-like or strychnine-like action, an assertion which, strangely enough, had been made only in quite isolated instances, the general consensus of opinion being in accordance with these particular results of laboratory investigation.

We are far from denying the importance and value of laboratory research, provided that the theoretical worker does not exceed his authority and does not presume to dictate to the clinician what he shall or shall not employ in the treatment of his patients. The laboratory worker has accomplished his task when he communicates the results of his investigations and when he has presented his own tentative conclusions as regards the clinical use of the drugs or remedies under consideration. The acceptance of these conclusions rests with the clinician who is in no wise obliged to bow to the *ipse dixit* of the laboratory worker when his experience and observation differ from the result of theoretical investigation. In making this assertion we are in accord with Dr. A. P. Francine (*New York Medical Journal*, 1910, June 18, page 1285), who declared that a good piece of clinical work is quite as scientific in

principle as a good piece of laboratory work, and the best type of clinical teaching is just as scientific as the same type of laboratory teaching. While we admit that in bedside observation it is exceedingly difficult to draw unbiased inferences, that a *post hoc ergo propter hoc* reasoning is all too tempting, we assert on the other hand that clinical observation may by no means be neglected in favor of the results of laboratory investigations, and we need only call attention to the fact that from Hippocrates down the clinical or empirical mode of study has been practically the only guide of physicians for many centuries, and that it has produced results which we of today, with all our laboratory methods, find it often difficult to surpass or even to equal.

The results of clinical observations with cactus grandiflorus and the claims which are consequently made regarding its action, point to the fact that it is of particular value in functional affections of the heart, while it exerts but a slight and secondary effect upon organic cardiac disturbances. Furthermore, the action of the drug is probably exerted far more upon the innervation, more particularly upon the sympathetic nerve plexus of the heart, than upon the heart muscle. Furthermore, experience has shown that cactus does not, like digitalis or strychnine, lengthen, intensify or increase the degree of ventricular or auricular contractions. It has been found by experience to work more particularly in conditions in which the action of the heart was uneven, irritable, excessive in rate or the reverse. In fact, it has been found to act essentially as a regulator of the functionally disturbed work of the organ.

All these experiences remove the drug from the sphere of laboratory investigation and a further reason for this we find in the experience that a normal heart is not influenced in any way by the exhibition of cactus, while an irritable or abnormally acting heart is favorably influenced, with a tendency to regulating its work. This is by no means strange. Prof. George F. Butler has shown in a study on cactus (*American Journal of Clinical Medicine*, 1908, page 1043) that cactus is not the only drug which fails to exert an evident action upon the healthy organism, but does exert a very manifest effect upon the diseased body. Furthermore, experiments made on frogs and other cold-blooded animals, while enabling us to determine the toxicity of a remedy such as, for instance, that of digitalis or strychnine, do not in any way permit definite conclusions concerning the clinical use or the mode of action in human or even mammalian patients. They permit, at most, tentative conclusions. The experiments which have been made on small

mammalians, and which have served to oppose the experience of the general practician in favor of cactus, did not fulfill the clinical indications for the use of the drug, because, as far as we can determine, with only one exception, normal animals were used for the experiments, and in that one exception, in a dog recovering from goiter, which therefore may be presumed to have had tachycardia, the administration of the remedy did not even pretend to adapt the rules established by clinical experience.

We must, therefore, conclude that the laboratory experiments which have been presented in the literature of the last three years in opposition to the therapeutic value of cactus grandiflorus and its preparations have not proved anything of merit or anything even worthy of further consideration, if it were not necessary to disabuse the minds of the blind worshipers of the highest science, socalled, which even in the best established laboratories sometimes deteriorates into pseudoscience, and if it were not desirable to support those clinicians who know from their experience at the bedside the merit and value of the drugs in question in their conviction, and to vindicate the use of the remedies.

Therapeutic Uses.—Thaddeus von Zelenski (*Klinisch-Therapeutische Wochenschrift* in June, 1902, cf. *New York Medical Journal* for September 13, 1902) studied the action of this drug in a large number of cases in which digitalis was not suitable, and his conclusions were very favorable. The dose in which the fluid extract may be used, Zelenski finds to be even greater than that recommended by others. Even if phenomena of intolerance appear, the appetite remains intact, there is no nausea or vomiting, while if the administration of the remedy is protracted through many days in succession, no cumulative result appears.

"The frequency of the pulse does not undergo any noteworthy modification; very often there is a slight acceleration accompanied by greater fullness of the pulse; so far no action on the respiration has been noticed. No harmful action on the kidneys has been observed; on the contrary, in all cases of heart trouble and of pleural exudation the amount of urine in twenty-four hours has been greatly augmented, but it is difficult to decide whether this result is due to a true diuretic action or to the improved functional action of the heart.

"The best results have been obtained in disease of the aortic valves, during the period of compensation. The author confirms Myer and Wilcox's previously recorded observations on this point. Dyspnea, arrhythmia, edema of the extremities, and ascites, which

nearly all these patients present, disappear speedily under the use of fluid extract of cactus; and at the same time the dimensions of the heart undergo a noteworthy diminution and marked improvement in all respects is evidenced.

"In mitral troubles the benefits are less clear; while dyspnea is lessened and the quantity of urine increased, the surprising results of digitalis are not attained; but cactus may be advantageously employed as a substitute for digitalis *during intermissions in its use.* In pleural exudations accompanied by cardiac debility, cactus, by improving the functions of the circulatory center and favoring diuresis, appears clearly indicated, and for the same reasons it is of service in infectious diseases in which the heart is more or less compromised."

According to King (American Dispensatory) cactus impresses the sympathetic nervous system, and is especially active in its power over the cardiac plexus. E. M. Hale says that it acts upon the circular cardiac fibers, whereas digitalis acts upon all the muscular fibers of the heart.

In medicinal doses cactus diminishes the frequency of the pulse, and increases the renal secretions, and is therefore sedative and diuretic. According to Scudder, it neither increases nor depresses innervation; so that it is neither stimulant nor sedative. Locke, on the other hand, believes it to be sedative, but not depressant. (Syllabus of Materia Medica.) In medicinal doses it does not appear to weaken the nervous system in the least.

The special field for cactus is found in diseases of the heart, in which it exerts a very decided action, palliating or removing the symptoms and frequently giving prompt relief. This influence upon the heart is manifested when the disorder is functional; organic conditions are only benefited in a measure. In the eclectic school, the drug is recognized chiefly as a functional remedy, and one of the best of cardiac tonics. There is no doubt but that the continued use of the drug tends to increase cardiac nutrition and waste, and in this way may benefit cases with structural lesions. The influence of cactus is exerted wholly upon the sympathetic nervous system, through the superior cervical ganglion, expending its force in regulating the action of the heart and controlling the cerebral circulation, thus giving increased nutrition to the brain. It is the remedy for almost all functional cardiac irregularities, as palpitation, pain, cardiac dyspnea, intermission in rhythm, etc. Even in structural heart-wrongs, the majority of unpleasant symptoms are due to disordered innervation, and this condition is cor-

rected by cactus. It does not seem to make any difference whether the heart-action is feeble, violent, or irregular, provided it be due to lack of innervation, associated with mental depression, or in excitable or nervous individuals, the remedy relieves, because its tendency is to promote normal rhythmic action of the cardiac muscle. In spasm of the heart-muscle, and in cardiac pain of a constrictive character, as if the organ were held with a strong band, it is the most prompt of all cardiac remedies. It is a good remedy in the heart troubles produced by tobacco.

Dr. Roland G. Curtin of Philadelphia, at a meeting of the American Therapeutic Society held in Philadelphia, May 7, 1908 (*Therapeutic Gazette*, 1908), spoke of cactus as in a class by itself, not like any other heart remedy. He was primarily led to the use of the drug by a report of the elder Flint. He said it was a mild tonic stimulant, acting especially on the inhibitory nerves and useful in relieving the heart of some of the unpleasant symptoms, met with particularly in the nervously disturbed heart; steadying and supporting it, even, at times, in serious nervous disease of the organ; that in any case it might relieve the discomfort and pain in the region of the heart. He also stated that it was a valuable adjunct to other heart remedies; but it was to be borne in mind that it was not a strong cardiac tonic or stimulant, and therefore not to be depended upon singly in a seriously diseased heart. With this conclusion most observers concur.

Dr. Solis Cohen said in an address before the Philadelphia Pharmaceutical Association (*Bulletin American Pharmaceutical Association*, Sept., 1910, p. 488, also *Critic and Guide*, Jan., 1911): "*The Journal of the American Medical Association* has published several articles to prove that cactus is pharmacologically inert; and some of them strongly imply that physicians who report good results from its use are unworthy of credence. Nevertheless I am neither afraid nor ashamed to appear in such excellent company as that of Dr. Roland G. Curtin, of Philadelphia, in support of the high clinical value of cactus, when a good preparation is properly used in suitable cases. Here is the point—a good preparation, properly used, in suitable cases. One who has not used a good preparation of a drug under discussion; or has not used it properly; or has prescribed it in a case for which it is not suitable; or one who has never used it clinically at all, is not in position to dogmatize as to its value. He may properly criticise, suggest, demand evidence. But he cannot properly condemn in the face of competent evidence in its favor; and it is the opinion, and not the drug,

that in such a case is to be considered worthless—or at least, needs to have its 'value established.' "

From the older literature on cactus, we refer to a report on "Drugs and Medicines" by Dr. N. S. Davis, to the Illinois State Medical Society in May, 1878, in which he stated that he had found the drug of decided benefit in cardiac palpitation, especially during the early morning hours. Dr. James I. Tucker, *Therapeutic Gazette*, 1880, page 40, considered cereus grandiflorus one of the very best remedies for functional derangements of the heart. He used cactus in the conditions which may be called "tobacco heart" and "tea" or "coffee" heart, as well as in cardiac palpitation of an emotional origin.

Dr. P. Watson Williams (*The Practitioner*, Vol. 47, No. 4) presented to the British Medical Association the results of a careful clinical study on cactus, which were emphatically favorable to the beneficial effects of the drug.

Dr. A. Orlando Jones (*British Medical Journal*, Jan. 11, 1890, page 70) found that while digitalis appears to be a drug that is more applicable to sthenic or overstimulated conditions of the heart, cactus grandiflorus appears to be applicable to asthenic conditions. He reported several experiences in support of this position.

The literature of the last thirty years could easily be culled to advantage for similar and even more decided experiences, but enough evidence has been adduced, we believe, to encourage those who (we will be quite conservative) believe to have obtained valuable and satisfactory results from the exhibition of cactus grandiflorus, to persist in the use of a remedy which can at least do no harm, since it does not possess a cumulative action, and which, in the experience of those best entitled to express an opinion, the clinicians, is of decided value in functional heart derangements.

The writer recalls two cases particularly which are of interest because they are apparently antagonistic, and serve to illustrate the satisfactory action of cactin.

Case 1.—Young lady, unmarried, twenty-eight years old, suffered from palpitation and irritable heart action, which had not yielded to various measures employed, including the usual heart tonics. Cactin, 1-67 grain, administered every fifteen minutes, quieted the irritation in the course of three hours. The patient has employed the drug at times during the last six years, always with the same benefit, and always and only for a few days at a time.

Case 2.—Lady, 73 years old, bradycardia, pulse 56, soft, easily compressed, precordial pain, anxiety, dyspnea on the slightest

exertion, the precordial pain occurring especially in the morning. She was directed to take one granule of cactin on awakening, and one after her breakfast, which was to be taken in bed. After three days the patient assured us that she was feeling very much better. The pulse was still slow, 58, the blood pressure had increased from 90 to 110. The quality of the heart's action was much improved. No other treatment had been given.

These two cases, considered side by side, illustrate the action of cactin as a heart regulator, and emphasize its importance in functional derangements of the organ.

We do not therefore claim that it stimulates or strengthens the heart beat, nor can we at present assert of our own knowledge that it either accelerates or slows the rate of the heart's action. The principal and most noticeable effect is a sedative one, an equalization of the cardiac contractions both in rapidity and in character. This justifies the indications which have been determined empirically. Cactin is not so much indicated in valvular disease or in enfeebled heart action, that is, not so much for a strengthening or stimulating effect, as rather in restlessness of the heart, in fluttering, palpitation, or in what has been described graphically as wabbly heart, for an equalizing, regulating and comforting effect. Given a patient who complains of an indistinct ache or discomfort in the pericordium, who tells you her heart "jumps so," that it seems to choke her, or again, given a patient with the capricious irregular heart's action that follows an over-indulgence in the weed, and a few milligrams of cactin repeated at brief intervals will have a wonderfully quieting effect, the ache and discomfort will disappear, the fluttering will cease. And what is of the highest importance for a long continued administration, cactin has not a cumulative action, and it does not disturb the digestion.

We cannot therefore call cactin a heart stimulant, nor is it a tonic in the strict sense of the word, which, according to Gould, is an agent which promotes nutrition and gives tone to the system. But if we admit with the Standard Dictionary that a tonic is a remedy that gradually restores the normal tone of organs from a condition of debility, we may argue that in unequal, irritated heart-action, due to a condition of debility (in whatsoever manner caused), anything which restores the equilibrium of this organ exerts a tonic effect, and in this sense we are justified in calling cactin a heart tonic.

Dose.—The dose of cactin must be adapted to the needs of the condition which we are called upon to treat. In tachycardia, or in

irritable, irregular heart action, we have found one granule every ten to fifteen minutes exert a markedly soothing effect in the course of an hour or two, after which the periods between doses may be prolonged until finally the remedy is given three or four times a day.

CAFFEINE

Standard granules—Caffeine alk., gr. 1-67, Gm. .001; caffeine alk., gr. 1-6, Gm. .01; caffeine arsenate, gr. 1-67, Gm. .001; caffeine benzoate, gr. 1-67, Gm. .001; caffeine benzoate, gr. 1-6, Gm. .01; caffeine citrate, gr. 1-6, Gm. .01; caffeine valerate, gr. 1-67, Gm. .001.

Caffeine has been found in the coffee of Arabia (Caffea Arabica), the tea of China (Thea Chinensis), the chocolate of Mexico (Theobroma Cacao), the guarana of Brazil (Paullinia Sorbilis), the maté of Paraguay (Ilex Paraguayensis), the kola of Africa (Cola Acumimata), and the yopon or Appalachee tea of the Carolinas (Ilex Cassine). All these plants and no others contain caffeine; all these, out of the myriads of plants produced by the earth, have been selected by the natives of these countries for use in hot beverages.

Is this simply chance? Or is it to be taken as showing that in caffeine there is some remarkable fitness to meet some unknown need of the human economy, some want unrecognized but nevertheless real, felt alike by these various races and by all mankind, savage, barbarous and civilized, in torrid, temperate and frigid zones, by the sea, on the plains, and in the mountains?

The caffeine used in medicine is obtained from tea leaves by sublimation, or by inspissation of the extract with alcohol, the tannic compound being first broken up by lead acetate. Chemically caffeine is trimethylxanthine. It has been formed synthetically. It is a weak base chemically, crystallizing in white, lustrous, flexible needles, soluble in 80 parts of cold and 2 of hot water, 50 parts of alcohol, 9 of chloroform, sparingly in ether. It is somewhat bitter. With strong mineral acids it forms easily decomposable salts. It does not form salts with organic acids and may be volatilized as caffeine from their mixtures. But with organic acid and soda salts, such as sodium benzoate or salicylate, caffeine forms double salts which are very soluble in water.

On frogs caffeine causes contraction with stiffness of the muscles, especially evident when a muscle is dissected out and immersed in caffeine solution, or when the latter is injected into the substance of the muscle. This is due to direct action on the muscle by increasing the fibrin ferment. All xanthine derivatives possess

this power, which is weaker when the methyl group is associated, as in theobromine and caffeine. The frog's heart resists the caffeine effect, continuing its rhythm after the striated muscles have stiffened tetanically.

Administered to warm-blooded animals in non-toxic doses, reflex irritability is increased from above downwards, the animal starts at every touch, and becomes tetanic at times even without evident cause. The psychic area is first stimulated, then the vasomotor and respiratory centers, later the reflexes are heightened and tetanic convulsions induced (Sollmann). Small doses increase the pulse-rate; larger doses render it irregular and slower till the heart stops in diastole. This is due to a direct stimulation of the cardiac accelerator apparatus and not to paralysis of inhibition, for under atropine the same effect is manifested.

Small doses increase vascular tension, larger ones depress it. The former effect is due to direct excitation of the heart and of the vasomotor center, contracting the peripheral arteries.

Respiration is quickened at first, inspiration becoming deeper; later it becomes slower. This action resembles that of strychnine.

The temperature rises about one degree F. after medium doses, and between two or three degrees after toxic doses. This is doubtless due to the muscular stimulation and increased vasomotor tension.

No effect upon peripheral nerves, motor, or sensory, has been determined after caffeine was administered internally in ordinary doses; but steeping a motor nerve in caffeine solution or injecting the latter around a sensory nerve produces rapid paralysis of function.

The lethal dose of caffeine for dogs is about 1-5000 of the animal's weight. Cats require double this dose.

The action of caffeine on the kidneys is complicated. The urine is lessened in quantity by contracting the renal arteries, when large doses are given. Small doses appear rather to stimulate the heart and increase the flow of urine. If the irritability of the nerves is lessened by chloral or paraldehyde, preventing the vasomotor tension, caffeine increases the excretion of urine. Liebreich credits this to direct irritation of the renal epithelium.

Metabolism is little affected. (Sollmann says it is increased.) The excretion of urea and carbonic acid is increased by the stimulation of muscular contraction. No material changes of the blood have been noted.

In man small doses up to Gram 0.1 (gr. 1 1-2) slow the pulse somewhat. Larger doses cause toxic symptoms, tinnitus aurium,

tremor of the hands, temporal pulsation, headache, flashes, vertigo, insomnia, mental confusion or delirium, amblyopia and transient deafness, palpitation of the heart, rapid pulse, irregular heart-action, and a sense of oppression in the chest. Some cases present erections, strangury, dysuria, anesthesia of the throat and tongue, with swelling and muscular stiffening up to the production of tetanoid spasms. Sometimes alarming heart-symptoms follow, even after small doses, especially in myocarditis. There are no cumulative effects, but idiosyncrasies against caffeine may exist. Larger doses are well borne by those accustomed to the drug. In any case, the alarming symptoms quickly subside, the caffeine being rapidly eliminated by the kidneys and liver or broken up in the body.

Caffeine is readily absorbed by all the mucosa and by the cellular tissues. Urea may be split off from caffeine, as the excretion of the former is increased while taking caffeine. The latter is found in large part unchanged in the urine, and a part as monomethylxanthine.

Experimenting on healthy men it is necessary to give doses of at least five grains to obtain appreciable results, allowing for idiosyncrasies, and, possibly, for the habitual use of coffee and the consequent resistance. Kelp gave eight grains to a nervous woman, with toxic effects disappearing within twenty-four hours; such as vertigo, sense of general fatigue, precordial anxiety, rapid pulse, abdominal pulsation, followed by trembling of the extremities, grinding of the teeth, later by heaviness of the head, and spasmodic contractions of the muscles of the neck and nucha.

But Frerichs, after taking a dose of 30 grains, felt only heaviness of the head, congestion of the brain, and vomiting, quickly followed by disappearance of the other symptoms. It is probable that the whole of this dose had not been absorbed.

Men may accustom themselves to ascending doses of caffeine; and the gravest symptoms of over-doses soon disappear.

Caffeine stimulates the striated muscular fiber, which explains the imperious need of emptying the bladder after drinking coffee, and why coffee removes the sense of fatigue after long marches.

Caffeine penetrates the organism rapidly, its effects are evanescent, its elimination rapid, by the bile and the urine.

Leblond, studying a hernia, found that caffeine augmented the muscular contractility of the intestine. Hannon and Peretti found it excited the intestinal secretions and even caused diarrhea. Leven and others credited it with favoring the secretions of saliva and of bile. Gubler and others found it provoked an abundant diuresis.

Small doses augment, toxic doses paralyze, respiration.

The pulse is lessened in frequency, increased in power; the blood-pressure raised by vasomotor contraction; and toxic doses cause the pressure to fall rapidly.

The observations on the body heat are contradictory, some testifying to a rise, others to a fall. Caffeine is a powerful stimulant to metabolism, and when the temperature is subnormal from deficiency of this function, caffeine will raise the heat to the normal point. This action I have frequently seen in studying persons who had discontinued the use of morphine. In a few months there is a notable fall of temperature, with oppression of the chest, and various unpleasant subjective sensations, which are relieved by quickly flushing the emunctories and giving caffeine. So also when the temperature has been depressed by exposure to cold, coffee will raise it to the normal point more quickly than the same quantity of hot water alone. But in fevers the same agent will not elevate the body heat, but even lowers it sensibly.

The effect on urea is obscure. The excretion is lessened, but this is probably due to the conservation of tissue, lessening waste. Lehmann and Froehlich claim that caffeine retards the decomposition of organic elements. Voit denied this, and declared that it does not modify the excretion of urea. Roux found that in his own case it increased the excretion of urinary solids, especially urea and chlorides, but on the establishment of the "coffee habit" the excretion returned to the normal. But Binz wisely remarks that the elevation of temperature contradicts the diminished excretion of urea. Caffeine must increase the loss of urea and of carbonic acid. Nothnagel says the metabolism (organic exchange) is not notably influenced by caffeine; and as applied to healthy men this is probably correct. Raphael found that half a gram of caffeine increased the quantity of urine 42 percent more than an equal bulk of hot water without the caffeine had done. The increase of solids was proportionately smaller. That it lessens the retrograde metamorphosis of body cells is clear.

Burggraeve said: "It is certain that caffeine, like the alkaloids in general, hinders combustion. This is especially the case with caffeine arsenate. We know how rapidly fever emaciates, and how soon fever falls after a dose of black coffee. When quinine has been scarce, intermittents were broken by coffee. Whence this fever? An exaggerated combustion, an elevation beyond measure of the animal caloric, greater when the fever presented marks of malignity or ataxia. We ourselves tried it, being heated, the body deranged,

bile lessened, when caffeine arsenate rapidly reestablished this secretion and lessened the uric acid in the urine.

"A boy with a wounded knee had fever of 40 C., ataxia, pulse 130, odor of mice, urine scanty and loaded with urates, exaggerated combustion and visible wasting. The urine contained 3.4 percent or urea. Thirst being normal he drank only the usual quantity of liquids, and took four daily doses of caffeine arsenate, three granules each. From the first day the effect on calorification was manifest, fever fell, the skin and tongue became moist. The bowels opened more freely, and in three days the improvement was notable. Veratrine was given for the accesses of fever due to the wound, these medicaments not excluding each other. The urea fell to 1.4 percent.

"Urea is a sort of cinder. In fever the operations of nature are simply accelerated, the denutritive combustion augmented, more cinders produced, and the kidneys cannot eliminate them fast enough. We arouse the vasomotor nervous system from torpor by the alkaloids and retard combustion by the arsenates."

This alkaloid is notable for the enormous proportion of nitrogen it contains, the formula being $C_8H_{10}N_4O_2$.

In small doses Laura pronounces it an excellent incitant of the nervous system. This term "incitant" is a favorite with European writers, they drawing a distinction between an "incitant," which promotes the normal exercise of a function, and an "excitant" which provokes activity that may be abnormal, excessive or undesirable in other ways. The distinction is worth preserving.

In toxic doses caffeine induces convulsions, causes debility, followed by paralysis and death by asphyxia. It acts especially through the spinal cord, of which it in small doses augments the reflex action and activity, and of which it maintains, by repeated small doses, the nervous energy, supplying this even when it is wanting in pathologic states.

Leblond's experiments led him to these conclusions:

1. In small doses caffeine is very well tolerated. It then, instead of provoking insomnia, becomes a veritable hypnotic.

2. It regulates the heart, augments the force of the impulses, and relaxes it when its action is excessive.

3. It is the best succedaneum to digitalis, to which it is preferable in grave cases when death is impending, because the action of caffeine is more prompt and sure; also when digitalis is not well tolerated or must be suspended. This, however, applies to those who still employ digitalis, not to digitalin.

Nothnagel found caffeine hydrobromate well borne, and acting well on the heart, to which it gave force, with asystolia, diminution of sanguine pressure and diuresis. He states that it acts as a diuretic in other maladies, in exudative pleurisy, pericarditis, hydropericardium and even in nephritis. It corrects arrhythmia.

Laura says that in fevers caffeine appears to lower the temperature; it acts as a tonic to the heart, and proves quite serviceable in albuminurias, cardiac and otherwise. It also seems to act on the contractility of the intestinal musculature in strangulated hernia. We know the happy effect here of hyoscyamine, alone or with strychnine, if with the spasmodic element there is also paresis and want of equilibrium between the circular and the longitudinal fibers.

Gubler showed that caffeine and the identical or closely analogous alkaloids of tea, guarana, theobroma, etc., share the diuretic power. They should be classed among the diuretics that stimulate the nervous apparatus of the kidneys.

Sclavo also found that caffeine possessed to a remarkable degree local anesthetic power over the mucosa, and surfaces recently burned or wounded.

Caffeine, even in doses up to five or seven and a half grains, does not as a rule cause insomnia, which is due to caffeone, the volatile principle of coffee. In acute nephritis caffeine may be used as a diuretic in cases where the vascular pressure is nearly normal; in cardiac asystolia it should be preceded by digitalin.

Caffeine is rapidly eliminated by the kidneys. It is not suited to cirrhosis of the liver, although well borne. Huchard advocated it in fatty degeneration of the heart-muscle, but it is not suited to the hypertrophic period; in the later stages of debility it is well associated with strychnine arsenate. Riegel designated caffeine as "a regulator of the heart."

The action of caffeine upon the brain is that of a strong excitant, quick in getting to work. Nevertheless it will not replace digitalin. In truth it is doubtful if any medicament can replace any other. As we study more carefully our drugs we will find each is better suited to some conditions than others. Each remedy is a distinct pharmacodynamic unit.

Caffeine, like coffee, does not do well with the gouty. In small doses it augments cerebral activity and muscular energy, renders the spirits gayer, more apt to mental labors, the body more lively. In doses of half a grain it is sedative. While it acts on the kidney it does not increase the output of urea, but diminishes it.

It facilitates the metabolic exchanges of the blood. It increases the biliary secretion and excretion (Liebig), with adults or children. The latter tolerate caffeine perfectly in suitable doses, and in them especially it augments the nervous and muscular activity of the stomach and the intestine. Laura insists that it lessens organic waste and stimulates assimilation; hence its value in convalescence from grave diseases, in athrepsies, tabes, and consumptions unless quite advanced, in which case but little benefit is to be expected.

Laura thinks that small doses of caffeine excite the sexual appetite, and it is in strict harmony with this that the abuse of coffee proves anaphrodisiac, over-stimulation exhausting the functional activity.

Synergists of caffeine are, theobromine, strychnine, quinine, and in some respects digitalin and the arsenates.

Morphine antagonizes caffeine, but when the latter is given as Burggraeve advises, morphine may be added to prevent or relieve insomnia, without interfering with the action desired. Nevertheless caffeine is the best antidote to morphine.

Therapeutics.—Caffeine is the appropriate remedy in myocarditis, functional heart-diseases, and in all cases where a quick and lasting heart incitation is required.

Headaches in chlorotics, and hysterics' migraines, are relieved by caffeine. The effect on neuralgia is uncertain.

In 1864 Botkin and Koschlakoff prescribed caffeine in dropsies, and in 1880 Leech recommended it especially in dropsy attending organic heart-diseases. Lepine, Huchard and Leblond followed, and finally Riegel ranked caffeine with digitalis. Based on 21 cases where caffeine was given alone or with digitalis, he deduced the following conclusions:

1. Caffeine shares with digitalis a regulating power over the heart.
2. In proper doses caffeine augments the heart's energy and retards its action, increasing arterial pressure.
3. It quickly provokes a notable diuresis.
4. The indications are the same as for digitalis.
5. The best mode of administration is by small doses often repeated.
6. It excels digitalis in an action more rapid and non-cumulative.
7. It can be given with benefit where digitalin is inactive.
8. The simultaneous use of narcotics like morphine is not to be recommended.

9. In general, caffeine is as well and often better tolerated than digitalis. The double salts of soda with benzoic, salicylic and cinnamylic acids, are especially commendable from their extreme solubility and facility for hypodermic use.

Liebreich recommended caffeine in fevers with weak heart, especially in edema of the lungs, as a heart-tonic and diuretic; also in renal and cardiac dropsies. In valvular affections he preferred digitalin and strophanthin. But when the heart-muscle no longer responds to the usual stimulants caffeine may be given with advantage. This applies as well to the treatment of renal diseases.

Zenetz dissents strongly from this use of caffeine, which he stigmatizes as treacherous, and deadly in large doses from sudden stoppage of the heart in systole. He found caffeine in the urine fifteen days after its administration ceased. Remedies should not be repeated while still in the body and necessarily exerting an effect. This causes cumulation. The more the kidneys are diseased, the slower is the excretion of caffeine. If extensive, any active remedy will accumulate. In fact the task of the day is to ascertain how powerful remedies once taken into the body are going to get out of it. And in this the vast importance of kidney-elimination must be recognized.

But the wholesale condemnation of digitalis is wrong.

We are often compelled to combine with caffeine and digitalis, strychnine in cardiac insufficiency with dyspnea, or hyoscyamine if there is a spasmodic element. In fevers with rapid wasting some form of arsenic is to be added, the arsenate of caffeine being eligible.

Caffeine has proved a sovereign remedy in certain forms of headache, migraine, hemicrania, with throbbing arteries (Burggraeve); those of chlorosis, or symptomatic of hysteria, and those where there is general aching not associated with hyperesthesia of the scalp (Rossbach).

How does it cure headache? We will wait, says Schmiedeberg, till we know the exact nature of the malady.

The stimulant effect of this agent on the cerebral cell is shown in cases of intellectual and nervous torpor; in coma, somnolence; in the state consecutive to long loss of sleep, from sunstroke, alcohol or the abuse of narcotics. In typhoid coma, and in the somnolence that accompanies the profound anemia of hemoglobinuria, caffeine arouses the brain.

In military service caffeine is of inestimable value in enabling the soldier to endure long marches with little food, that he could

not possibly have endured without it. Strychnine is an aid here. In removing the sense of hunger and of fatigue caffeine approaches cocaine; in stimulating the nerve-cell and the muscular fiber it ranks with strychnine.

Burggraeve called attention to the value of caffeine in relieving the accidents due to the abuse of tobacco, and to its cholagog power. Caffeine arsenate neutralizes the stupefying effects of tobacco, and relieves the asthma, dyspnea, dyspepsia, cerebral congestion, and intermittent neuroses, caused by tobacco. In catarrhal and rheumatismal jaundice he insisted on general baths, with mild laxatives, and restored the secretion and discharge of bile by the use of quassin and caffeine, esteeming them the best since they cause no intestinal irritation; and as Liebig said, caffeine augments the taurin. The depression of the pulse does not permit the other alkaloids; unless in continued fever when veratrine and aconitine are needed, especially with cutaneous hyperesthesia. In spasmodic jaundice it is atropine that is needed; but if the spasm depends on weakness one can give strychnine or brucine, alone or with quassin and caffeine. In malarial jaundice we must insist on quinine, with quassin and caffeine to restore the bile. Watch for the proper time and do not force the remedy.

Olliviers has reported two cases where caffeine exerted an anthelmintic action, in children.

Eulenberg used caffeine hypodermically, for neuralgias.

The effect on the contractility of the intestinal muscles has led some to try it in strangulated hernia.

In continued, intermittent and adynamic fevers, several have used coffee; and others have given it with success in asthma.

Caffeine is useful as a cerebral stimulant when sleep must be postponed; it is applicable in cerebral torpidity, in accidents, sunstrokes of the heat-exhaustion type, coma, somnolence and hemicrania. As a sustaining force during prolonged mental efforts or during prolonged and fatiguing manual labors, to postpone or remove the sense of fatigue, caffeine is the most useful of remedies. It seems to be a nerve food in such cases. Laura uses it with immediate benefit in nervous palpitations, especially hysteric, and in organic cardiopathies with regular rhythm but a heart-action at once very rapid and very feeble; also in many ill-defined cases of nerve-disease, more or less painful. In hemicrania he associates it with aconitine and gelseminine; in asthma with other antispasmodics and vital incitants, and here the success will be the more marked as the heart-action is the more wanting in energy.

Moderate doses relieve hiccough, and priapism. The valerianate is the best form as an antispasmodic. Passive congestions of the brain, the stuporous states of typhoids, or of alcoholism, call for the citrate—a bad preparation, universally condemned as a variable mixture, not a chemical union. In depressed states of the nerves, general debility and fatigue of the heart-muscle, the arsenate of caffeine may be associated with strychnine arsenate, atropine and digitalin (Laura). The author last quoted employs caffeine as a general stimulant, to increase biliary secretion, to reestablish stomach digestion and regulate the intestinal functions in acholia; in gastric and enteric dyspepsias with habitual diarrhea; and in infants reduced to a state of marasmus, athrepsia and atrophy, of which so many cases are to be seen among the poor of great cities. Good hygiene, iron, arsenic and the phosphates should not be neglected. The effects of caffeine are striking in obstinate duodenal and ileocolic dyspepsias; when, the hepatic function being deficient, too little bile is supplied. It excites the stomach activity in torpid conditions, stimulating the gastric nerves, provoking peristalsis and probably activating the secretions, thus perfecting digestion. The abuse of coffee induces dyspepsia; moderate quantities may occasion acidity.

Pure caffeine may be administered for many days in full doses. Of the arsenate 20 granules or more, each 1-67 grain, may be given to an adult *per diem*, if required. Of the citrate gr. 1-6 may be administered every quarter-hour until effect. This is preferable in every way to the bulky doses recently advised. The valerate is a valuable antispasmodic and acts best in small doses—gr. 1-67 every ten minutes, though even Laura, who greatly lauds small doses, speaks of 5-grain dosage on occasion.

In treating drug and alcohol habitues large doses are needed.

Caffeine will never be appreciated as a remedy until we realize that it is not simply "coffee." Were this potent berry looked on more as a drug and less as a food it would be better all around. The writer has occasionally, when compelled to continue his labor into the night beyond his usual hour for sleep, employed the little granules of caffeine, 1-67 grain, instead of the much larger dose contained in a cup of coffee. It is edifying to find how little a dose of caffeine will do the work when taken in this way, a single granule whenever one gets sleepy. One great advantage is that when the task is completed one is not kept awake longer by the overdose of coffee; but sleep follows quite naturally, the force of the caffeine having been spent. To travelers, campers, hunters, etc., these

granules supply all the sustaining qualities of coffee, when dissolved in hot water, without the flavor—or the weight.

The difference between the use of crude plant products and the pure active principles is exemplified in the caffeine beverages. Sollmann says that tea contains 10 to 21 percent of tannin, rendering it astringent, interfering with digestion and checking diarrhea; lessening absorption and precipitating proteids and albumoses. The irritation of small doses may be beneficial. The tannin is extracted slowly so that the longer tea stands the worse its effects. The aroma is due to volatile oils (1-2 to 1 percent), and these escape with the steam. They add to the flavor and stimulate the brain. Green tea contains more of these than the black. The hot water is a reflex stimulant, diuretic and diaphoretic. Tea should be quickly infused with boiling water and poured off the leaves. The best teapot is one rarely seen, with solid top, retaining the aroma. Tea contains 1 to 4 percent of caffeine.

Coffee contains 1 to 2 percent of caffeine; 15 percent of sugars, 13 percent each of fats and proteids. It has more tannin than tea, but differing in its quality, as it does not precipitate proteids and is but slightly astringent. It does not interfere so much with digestion but is even more harmful than tea, in some forms of dyspepsia, from the action of the caffeole, an empyreumatic oil formed in the roasting. This contains about 50 percent of furfurol alcohol, and a little phenol, valerianic acid, etc. It is a local irritant to the stomach, and slightly laxative. Coffee seems to excite gastric fermentation in those subject to it, and pruritus. In overdoses it acts as caffeine. Those who are in the habit of drinking excessively strong coffee in the morning are apt to have headache, lassitude and vertigo if they miss their accustomed dose. Nevertheless much of the recent prejudice against coffee has been excited by interested parties who have substitutes to sell.

Chocolate nuts contain about 50 percent of fat, unusually difficult of digestion. How much of this is in the chocolates of commerce depends on the manufacturer. The cocoas have only a portion of this fat removed, as may be readily demonstrated by washing with ether. The alkaloids are caffeine, 0.35 percent, and theobromine in widely varying proportions. The latter is also present in the shells, without the fat. The seeds also contain 5 percent of cocoa red, 15 percent of starch and as much proteid, and 0.6 percent of sugar, with an unknown volatile and odorous principle. The stimulation is less marked than that of tea or coffee, but to those who can digest the fat it is that much more nutritious.

Maté, the Paraguay tea, contains more caffeine than either tea or coffee, some tannin of an innocuous variety, and only a trace of volatile oil. It is deficient in flavor therefore, but contains all the comforting and tonic powers of the better known beverages. Those who learn to use it usually prefer it to the others, and many invalids who can not employ tea, coffee or chocolate enjoy their cup of maté with impunity. Repeated efforts have been made to bring this beverage into the market but without success. It only needs some lucky accident to give it "vogue."

The psychic and respiratory stimulation are due to the volatile oil and are secured from green tea especially, and lost when the alkaloid is substituted. Diuresis is partly due to the water. Some stimulation of the muscles, including the heart, is also to be accredited to the oils. Granules of caffeine dissolved in hot water afford all the diuresis, nearly all the sustaining properties and the relief from the sense of fatigue, in fact all the real benefits of the caffeine-bearing beverages except the euphoria—and part of this is due to the hot water. The use of the granules does away with all the objectionable features of these beverages. Sollmann says that caffeine in moderate doses does not seem to become noxious with habitual use. The excessive use of these beverages is apt to do most harm by disturbing the digestion. For the diminution of mental or muscular fatigue he advises well-roasted coffee or green tea briefly infused; also to induce wakefulness. Coffee relieves the sense of hunger temporarily but really increases metabolism and consequently waste. The calorific value of the sugar usually taken with these drinks should not be overlooked.

The hypodermic administration of caffeine presents many advantages—in coma, narcotic poisoning, irritable conditions of the stomach, and when the local analgesic effect is desired in treating neuralgias.

Dosage.—Dujardin-Beaumetz and Huchard have given caffeine in doses up to gr. 45, thrice daily; the latter limits the useful dose to 18 grains. These doses are toxic and are not to be advised. Six grains have produced toxic effects, and 7½ grains occasioned convulsions (Sevestre).

When we get rid of the idea that the proper dose is all a patient can take without actually killing him, and learn to measure our doses by the effects to be secured, we find that caffeine itself is best given in doses of a grain, singly, and up to seven grains a day, while the arsenate is most useful in granules of gr. 1-67 each, and rarely more than seven to ten of these in twenty-four hours. The

citrate of caffeine is too uncertain for accurate medication. The same might be said of the valerianate, but this is the most actively diuretic of the caffeine salts, and in doses of a grain has proved on many occasions its great value.

In treating the subnormal temperatures of men formerly morphine addicts, the hypodermic dose of three grains once or twice a day was rarely exceeded by the writer, and this much was not often required. In fact, in treating headaches of great intensity, gr. 1-6 every ten minutes rarely fails to give relief within an hour or two, if this remedy is indicated. If due to autotoxemia, it may even relieve before the bowel has been emptied of its poisonous contents, but this is not good practice.

As a cardiac tonic, from 1-6 to one grain should be given every hour till the required tonicity is secured; and in view of the rapid excretion of caffeine this is better than less frequent larger doses.

In wasting fevers Van Renterghem recommends the arsenate up to 20 granules a day, each gr. 1-67. In prolonged deprivations of sleep it is of the utmost importance to give just enough and not any more; so that the little doses frequently repeated as per the need are excellently calculated. So also for soldiers on the march; use just enough and no more, and good will result; give too much, exhausting the susceptibility of the system, and disappointment must ensue.

In nicotism Burggraeve recommended the arsenate, ten to twenty granules a day, the patient moderating or ceasing the use of tobacco.

Liebreich gives the dose of caffeine in hemicrania as Gm. 0.1 to 0.2 (gr. 1 1-2 to 3), in heart-weakness as Gm. 0.05 to 0.1 (gr. 5-6 to 1 1-2), every hour or two; and Gm. 0.6 to 0.8 (gr. 9 to 12) as a daily dose. It may be given in wafers, pills or pastilles.

When giving caffeine to young persons showing nervous irritability, it is best to administer the daily dose in the early part of the day to avoid insomnia.

The daily maximum dose is variously stated by European pharmacopeias as Gm. 0.5 to 1.5 (gr. 7 1-2 to 23).

For hypodermic use the double salts are preferable on account of their great solubility. Of caffeine alkaloids—

The caffeine-soda			benzoate	contains	46	percent	of	caffeine
"	"	"	cinnamylate	"	62.5	"	"	"
"	"	"	salicylate	"	62.5	"	"	"
"	"	"	hydrochlorate	"	52	"	"	"

The salicylate may be prepared easily by taking 35 grains sodium salicylate, 40 grains caffeine, and distilled water to make two drams, of which three minims contain one grain of caffeine.

For hypodermic use this should be made with chemically pure sodium salicylate; that of Schering being the only one I have found that gave a colorless, unirritant solution. This should be injected the moment it is taken up in the syringe, or the metal of the needle will be acted upon and will contaminate the solution. The syringe should be washed at once after being used.

The arsenate of caffeine is an excellent preparation, an excitant and tonic to the nervous system, which it calms indirectly by increasing its vigor. States of decided feebleness may be manifested by disorders of the centers of motility and of sensation as well as of the nerves and the organs under their control. It is in reestablishing the circulatory and nutritive processes of the nervous apparatus that many of the dynamic modifiers act as calmants.

Burggraeve termed caffeine arsenate a *vital retarder*. It diminishes organic combustion and is very efficacious in the fevers of pulmonary consumption. While we can not cure the advanced forms we can at least prolong life and render it tolerable; for much of their suffering is to feel themselves consumed. Under caffeine arsenate the pulse and the heat moderate and the gallop slows.

Laura advises caffeine arsenate in all ataxic and adynamic conditions. This sustainer of the cardiac forces and regulator of the cardiac centers and nerves finds numerous applications without at all exaggerating its value.

Burggraeve used this salt in nicotinism, with good effect.

Laura says that caffeine **valerate** exerts all the physiologic power of caffeine, especially affecting the gastrohepatic function. Paret found that it augmented the digestive powers and the muscular force. Nervous vomiting is readily controlled by it. Laura advised its use in hiccough, especially when coming immediately after a meal, adding also strychnine arsenate. Labadie-Lagrave vaunted it in whooping-cough as an antispasmodic, and Laura extended the indication to cover all forms of hyperesthesia and spasm of the respiratory passages, especially in women and children. Leynoux found that in whooping-cough it diminished the violence of the paroxysms and lessened their frequency. It is a good adjuvant to *calx sulphurata*.

The granules contain 1-67 grain each. Laura advises 20 to 40 granules a day to adults, and more if needed, running the daily dose on occasion up to five grains.

Caffeine-sulphuric acid forms salts that are said to have no vasomotor tensor power whatever, while they exert the diuretic properties of caffeine to the fullest extent. The sodium, lithium

and strontium caffeine sulphonates are known as symphords. They are soluble in cold, more rapidly in hot water; the solutions are not permanent. They have proved efficient diuretics in dropsy, obesity and fatty heart, in doses of Gram 4.0 to 5.0 (gr. 60 to 75) *per diem.*

Bromo-caffeine, $C_8H_9BrN_4O_2$, is produced by treating caffeine with bromine at a slowly rising temperature.

Ethoxy-caffeine $C_8H_9(OC_3H_5)N_4O_2$. The introduction of the ethoxyl group adds to the cardiovascular tensor effect of caffeine a narcotic property. It has been given in doses of Gram 0.2 to 1.0 (gr. 3 to 15), in hemicrania and trigeminal neuralgia. Collapse with vomiting followed doses of Gram 0.5 (gr. 7 1-2). It must be given therefore with caution.

Satterthwaite says: "Caffeine mildly but rapidly stimulates the circulation. Its effects are felt in a few minutes. It is, therefore, adapted for cases of heart failure. It causes cardiac compression and increases arterial pressure. It is more useful as an adjuvant than alone. It is especially well combined with glonoin, where it unites diuretic effects of the one with vasodilation of the other. In large doses caffeine has been known to bring on fatal cardiac contraction. Three-grain doses three times a day have done this. It is cumulative and its effects are felt for many days, so it should not long be continued. I give it in half-grain doses, with one grain of sodium nitrite, but do not continue longer than a week. A reliable alkaloid should be obtained."

Vahlen, in the *Enzyklopœdie der Praktischen Medizin*, Wien, 1905, says that caffeine strongly excites the central nervous system. In frogs and mammalia it produces tetanic cramps resembling those from strychnine. In the human body the effect of small doses of caffeine on the centers shows itself in a peculiar influence on the temper of the individual, so that mental work becomes easier, preventing all tired feeling. Larger doses, Gm. 0.6 (gr. 9), and more, excite the cerebrum, producing dizziness, headache, tinnitus aurium, and a state resembling drunkenness which may progress to delirium, terminating in somnolence and stupefaction.

The good psychic effect of caffeine in the moderate use of coffee as a beverage is increased by its peculiar influence on the muscles. Not only does it increase the absolute power of the muscles, but it also enables them to do longer and greater work without exhaustion. It is only after absorbing greater quantities that we notice more difficulty rather than alleviation in the exertion of labor owing to a peculiar change taking place in the substance of the muscles, viz., a condition similar to that of the rigidity in death

and in that from heat excess. In applying caffeine directly to the muscle minimal doses only are requisite.

Caffeine also exerts an influence on the renal epithelium and increases diuresis; whether or not it increases the heart-action at the same time has not yet been fully ascertained by experiment on animals. In the human being caffeine acts similarly to digitalis in regulating cardiac action when there is a disturbance of compensation, and in this way causes the disappearance of edema.

In the healthy person even medicinal doses, Gm. 0.5 (gr. 7 1-2) will produce cardiac palpitation, rapid, ultimating in irregular pulse.

Coffee and tea as beverages though owing their stimulating action principally to caffeine still have from the roasted coffee certain volatile products, and in the tea certain ethereal oils which increase that action. These substances seem to act irritatively upon the cerebrum. Medicinally tea and coffee infusions are used in narcotic poisonings with alcohol and narcotic alkaloids, especially morphine, in which latter case the tannin in the tea helps also by combining with the alkaloids and making them inert.

Pure caffeine, which can be produced synthetically also, crystallizes from hot water in delicate needles, having the chemical formula $C_8H_{10}N_4O_2+H_2O$. It is difficultly dissolved in cold water, and is administered in powders, pills and tablets in migraine, headache and neuralgia. As a diuretic it is given in Gm. 0.2 (gr. 3) doses several times a day. Theobromine excels, however, caffeine in this respect. In the same dose it is given as a substitute for digitalis in heart troubles several times a day.

Instead of the badly soluble pure caffeine there are combinations of it better soluble. Caffeinum natriobenzoicum is easily soluble in water. It is a white amorphous powder, and is given in double the dose of caffeine. Its easy solution in water makes it possible to be given hypodermically, the initial dose being Gm. 0.1 (gr. 1 1-2) and the maximum dose Gm. 1.0 (gr. 15) *pro dosi*, three times a day.

CALCIUM CARBONATE

(CALCALITH—ABBOTT.)

Standard granule—gr. 10, Gm. 0.6.

Calcium carbonate is too abundant in nature to require description. Its principal employment in medicine is as a remedy for the uric-acid diathesis, and when so used it should be in the c. p. form.

We know essentially nothing positive in regard to the real primary cause of the uric-acid diathesis, but it is clear that any attempt to remove the consequences of this uric-acid accumulation must be directed (1) towards removing the excessive uric acid from the blood and tissues, (2) towards preventing the deposits of crystalline urates and, (3) towards attempting to re-dissolve these concretions after they have once formed. This brings us to the fundamental therapeutic question that has agitated physicians for over a century, namely, "What can we do to dissolve uric acid after it has been deposited and what can we do to hold it in solution so that it will not be deposited or redeposited?"

There are a great many socalled "uric-acid solvents," the leading ones being alkalies, the salts of lithium, colchicine, lysidin and uricedin. Now, as a matter of fact all that we know about these different bodies is that they possess the power of dissolving uric acid in a test tube, that is, outside of the body, and it is exceedingly questionable whether they possess the same power when circulating in the blood and tissue fluids. It seems hardly possible that they should be able to perform this function, for, when we administer a few grains by mouth, very little of these different bodies ever reaches the uric-acid deposits. One might as well expect to reduce obesity by administering small quantities of ether on the ground that ether is capable of dissolving fat outside of the body, or expect to dissolve the lime salts in osteophytes or calcareous tubercles by the administration of mineral acids, on the ground that these will dissolve lime salts in a test-tube.

There is finally another fallacy about all this (and this applies particularly to the administration of small quantities of lithium salts), the *lithium carbonate never enters the blood as a carbonate but as a chloride*, for as soon as it reaches the stomach the hydrochloric acid liberates the carbonic acid and forms lithium chloride, and the latter is not an active uric-acid solvent.

The uric acid in the blood combines only to a very slight degree with the lithium; the bulk of it is bound to remain in solution in combination with other stronger bases like sodium and potassium that are always present.

That all this is true, can be demonstrated by a very simple experiment: If we give a small quantity of lithium carbonate by the mouth it appears almost quantitatively in the urine within a short time, not, however, in the form of lithium urate but as lithium chloride. We see, then, the ordinary treatment of the uric-acid diathesis by socalled uric-acid solvents is based on a number of fallacies and

inconsistencies; in fact, to this time it has been largely shrouded in empiricism.

The question is, what can we do? And the answer is given in the following arguments: We must first determine what factors are operative to keep the uric acid in solution and we must then attempt to enforce these factors. This point has been made the subject of an exhaustive investigation by Dr. A. C. Croftan of Chicago. He explains how the sodium salts of phosphoric acid are concerned in keeping the uric acid in solution; how one series of these salts (the basic salts) dissolve the uric acid with the greatest facility, whereas another series (the acid salts) have a tendency to precipitate it. He puts it as follows:

"Phosphoric acid forms three salts with sodium, namely:

H_3PO_4, phosphoric acid;
NaH_2PO_4, mono-sodium phosphate;
Na_2HPO_4, di-sodium phosphate;
Na_3PO_4, tri-sodium phosphate.

"The mono- and the di-sodium phosphate normally occur in the urine. Uric acid is readily soluble in di-sodium phosphate, but it is not soluble in mono-sodium phosphate. The addition, in fact, of mono-sodium phosphate to a solution of uric acid in di-sodium phosphate will cause the precipitation of the uric acid.

"It is clear, therefore, that the solubility of uric acid in the urine is enhanced by the presence of di-sodium phosphate and that the tendency to the formation of uric-acid concretions, increases in proportion to the amount of mono-sodium phosphate that is excreted through the kidneys.

"It is also clear that any endeavor directed toward preventing the precipitation of uric acid in the urinary passages must be concerned with increasing the amount of di-sodium phosphate and decreasing the amount of mono-sodium phosphate.

"The ideal would be to cause the complete disappearance from the urine of mono-phosphate and at the same time to produce the elimination through the kidneys of a quantity of di-phosphate sufficiently large to hold all the uric acid excreted in solution.

"The regulation of the phosphoric-acid content of the blood can be achieved by the administration of calcium salts. For, in the first place, calcium forms insoluble salts with the alkaline phosphates contained in our normal food, and in this way prevents the absorption of this moiety into the blood. In the second place, calcium, owing to the great affinity it possesses for phosphoric acid, combines with the phosphoric acid encountered in the blood-stream, and is

subsequently eliminated in the form of calcium phosphate—*not, however, through the kidneys, but in great part through the intestine.* This is an important point, for in contradistinction to sodium, potassium and magnesium, all elements that are chiefly eliminated through the kidneys, 85 to 95 percent of calcium is eliminated through the bowel.

"It will be seen, therefore, that calcium given by mouth will, first, prevent the entrance of preformed phosphoric acid (phosphates) from the food in the blood, and, secondly, will prevent the phosphoric acid formed in the organism from passing into the urine by causing its elimination through the intestine."

One might ask if the salts of sodium, or potassium, which are also capable of forming basic phosphates in the blood, might not answer the purpose just as well as calcium? But, as Dr. Croftan clearly brings out in his article, there are certain objections to the use of the sodium salts. In the first place, sodium phosphate, in contradistinction to calcium phosphate, is excreted through the kidneys and not through the bowels, so that only very little would be gained by the administration of these sodium salts, unless so much were given that the gastric function would be seriously injured and the other effects produced that we know to follow the continued excessive alkalinization of the blood and the urine. The urine is normally slightly acid, and it should be kept so, and calcium salts given even in considerable doses never render the urine alkaline. Dr. Croftan summarizes these objections in the following words:

"Whereas, therefore, the administration of large doses of sodium salts for long periods of time may be indicated on theoretical grounds, it is contraindicated on empirical grounds. First, because it renders the urine alkaline and thus favors the deposit of concretions other than uric-acid stones; second, because it exercises a deleterious effect on gastric digestion; third, because it is not without effect on the corpuscular elements of the blood; fourth, because it is superfluous, as calcium salts, by decreasing the phosphoric acid of the urine, thereby cause a relative increase of the sodium (and of the sodium di-phosphate) without at the same time rendering the urine alkaline."

Therapeutics.—Dr. Croftan advises the administration of the carbonate of calcium in ten to fifteen-grain doses two or three times a day, together with a full glass of water. The results obtained from this practice in various manifestations of the uric-acid diathesis, gout, goutiness, rheumatism and particularly in gravel and nephro-

lithiasis are very gratifying. The results that Dr. Croftan publishes in his preliminary note are as follows:

"I report four cases; they present no clinical features of sufficient intrinsic interest to merit chronicling in detail. The only noticeable fact is that all four were advised by me several years ago to use calcium salts continuously; that all four were lost sight of for periods varying from two and a half to four years, and that all four recently again came under observation for other causes without having suffered a recurrence of their attacks of renal colic during the whole intervening time. Several other cases I have lost track of, but hope to rediscover.

"Von Noorden, who first advocated the use of calcium salts in nephrolithiasis, reports only two recurrences of renal colic among twenty-one cases; in one patient an attack occurred a few days after beginning the treatment; in another patient who had suffered from severe attacks every few weeks, an attack developed nine months after the treatment was begun, and not again thereafter.

"The good results obtained in my four cases and the statistics of Von Noorden lead me to believe that the treatment of uratic nephrolithiasis by the continuous exhibition of calcium salts is efficacious and deserving of extended trial."

This report has been supplemented by the experience of many physicians who verify these findings in detail. In all diseases of the uric-acid type, calcium carbonate (or its compound preparation, Calcalith) has been found efficacious. Such are not only rheumatism and gout, but sick headaches, myalgia, asthma, hay fever, nephrolithiasis, urinary calculi, eczema and other skin diseases, many nasal and throat troubles and a variety of other affections of this type.

It appears, therefore, that we have here at least a true physiological uric-acid solvent, and that, to judge from the reports of careful, conservative and at the same time scientific clinicians, the administration of calcium salts is of great value in the treatment of this class of disorders.

I have supplemented Croftan's investigations with a sufficient experience to justify me, as above in standing for his findings. I would even go further than he does in my claims for the efficiency of this experiment, but in so doing have added certain synergists and prepared a c. p. calcium carbonate which added to lithium and colchicine makes in Calcalith (Abbott) a remedy which, as an eliminative, is far superior to the plain salt, and the value of which is untold. *It is a true uric-acid solvent, stimulating every excreting*

organ and is applicable to every manifestation of the uric-acid diathesis.

CALCIUM IODIZED

(CALCIDIN.)

Standard tablet—gr. 1-3, Gm. .02.

The names "calcium iodide" and "iodide of lime" have long been known in chemistry and in the schools of medicine, yet these names are loosely used and do not always refer (and never properly) to the remedy to which we refer. This is an important point and must not be lost sight of.

The "iodide of lime," socalled, to which we refer (properly calcium iodized, or iodized lime, or Calcidin, A. A. Co.), is not the chemical crystalline salt, CaI_2; it is not a crystalline body at all and does not contain that definite molecular combination which that chemical formula indicates.

Calcium iodized is an amorphous compound body or substance containing a much larger quantity of iodine; which readily separates from its loose combination with the lime, when coming in contact with acids, and thus lets the nascent iodine free to do its absorbing and alterative work.

This salt and its peculiar and specific application to the treatment of true croup were discovered some years ago, and, as it was then erroneously called "iodide of lime," and "brown iodide of lime"—neither of which it is—it attracted little attention. Owing to this incongruous nomenclature it was left in its empiricism, and even the few who had learned to rely upon it did not attempt to explain the rationale of its action.

Physiologic Action.—While calcium is a valuable reconstructive it serves here mainly as a base or vehicle for the iodine to which we must look for the explanation of the peculiar therapeutic activity of the compound. The remedial power peculiar to iodine is to stimulate to renewed vitality the absorbent vessels of the body, which have become either pathologically impaired, or are insufficient in their normal state to take up and dispose of the adventitious matter which does not belong to the body normally. The difficulty with iodine is, that it cannot be given in its purity, even in medicinal doses, for any length of time without producing unpleasant sensations in the skin, nose, throat and eyes.

This, however, is less the case in children, who are naturally more tolerant of this remedy and become more and more so under

treatment, especially when it is given in the form of an iodide, and above all, when given as iodized lime, very likely because lime is a normal constituent of the body, thus carrying the iodine to it in a more natural and readily assimilable form. However this may be, the fact remains that calcium iodized does not often cause iodism, even when given in maximum dosage and for a prolonged period.

Therapeutics.—Croup, that sudden scourge of infancy and childhood, when it is merely spasmodic, that is, when the chink of the glottis is narrowed by a spasmodic contraction of the muscular and other fibers of the vocal cords, while amenable to and well treated by calcium iodized, can usually be overcome by antispasmodics. Of these, aconitine, hyoscyamine and apomorphine are the best. It is always well, however, to include calcium iodized, for diagnosis cannot always be sure, at first, between the true and the false forms of croup.

For a child up to five or six years, give about six tablets, gr. 1-3 each, or two to three grains of the powder, dissolved in six teaspoonfuls of water, a teaspoonful every five to ten minutes until effect, or one to three grains, dry on the tongue, following with a draught of water. If for any reason this is not efficient, recourse should be had to apomorphine (1-16 to 1-12 gr.), hypodermically, attempting to stop at nausea, just short of actual emesis—unless the latter be clearly indicated. In severe cases complicated by "a full stomach," the apomorphine may be given at once with advantage, Calcidin, Abbott, being exhibited in smaller doses as soon as emesis ceases.

But the same croupy cough may be caused by a catarrhal state of the inside of the larynx, tumefying the vocal cords, narrowing the chink between the true vocal cords, thus producing that peculiar "crow" and a moderate amount of dyspnea, which antispasmodics will not permanently relieve. The case may even proceed to an exudation of material capable of forming a membrane, not only on the vocal cords, but on the parts above and below them, and the danger of suffocation becomes imminent. It may not be easy in such cases to distinguish between a diphtheritic and a simple croupous membrane, and while we cannot be sure of the efficiency of this remedy in the former—for the simple reason that there we have a specific toxin to deal with—we are sure of it in the latter. Calcium iodized (Calcidin) properly and persistently administered will rarely disappoint, and most frequently it will surprise the physician with the rapidity of its action.

The following is the experience of one physician, as related in *The Alkaloidal Clinic:*

"About seven years ago I first used calcium iodized for membranous croup, since which time all difficulty in curing every case which has fallen into my hands has ceased, and I am firmly of the opinion that nowhere in the domain of therapeutics have we a remedy more deserving of the name 'specific.' *During these seven years I have treated not less than twenty-five or thirty cases of this fatal disorder, true croup, without a single failure and without remaining at the bedside of my patient for a single hour.* Under its use the symptoms quickly improve and invariably disappear, and the patient moves forward to an easy and sure recovery. The dread which I formerly had of this malady has entirely disappeared and I take charge of these cases with as much assurance of recovery as though the little ones were suffering only with measles."

Hundreds of similar reports in our files are conclusive evidence of the value of this remedy in croup.

It is important that no error in diagnosis be made, if satisfactory results are to be obtained from the use of the remedy, for while it is almost certain to cure any case of spasmodic or membranous croup in which it is used within reasonable time, it possesses alone no curative virtues in diphtheritic croup.

Calcium iodized is also praised by respectable authorities as an absorbent agent in cases of uterine fibroids, when given in small doses three or four times a day for months, and even for a year. It is also praised as a calmative remedy for the dyspnea that is likely to arise, at night, especially, from heart-disease. So also in the dyspnea of consumptives, and in that of asthma, where it is one of the very best remedies we possess. In fact, it may properly be used in all conditions where the iodine effect is desired; and that it will produce that effect with less irritation and with less expenditure of time than any other iodine-carrying agent with which we are familiar, the practician can speedily prove for himself by trying it a few times. It has been employed in syphilis when a quicker action than that of KI is required.

To young infants with the "snuffles," whether due to post-nasal adenoids, hypertrophied turbinates or inherited syphilis, given in doses ranging from 1-2 to 1-3 of a grain three or four times a day, as indicated, it will be found to quickly relieve, and, with removal of cause, will soon effect a cure. In older children with night cough, due either to catarrh of the nasopharynx, or to clogging of the bronchi in subacute or chronic bronchitis, doses of one-third to one grain, repeated every fifteen minutes for a few doses during the paroxysms, will often give relief when everything else fails.

Through its alterative action it favorably influences these cases when given continuously three or four times a day.

After grippal attacks, where the bronchial glands are enlarged and there is found upon examination of the throat, a tough, grayish-yellow secretion adhering closely to the folds of the soft palate and to the sides of the pharynx extending into the vault, and in which there is a disagreeable, dry, rasping cough, calcium iodized in doses of one or two grains, dissolved in water, and given every quarter or half hour, will act promptly and afford relief sooner than any other remedy yet tried. In all catarrhal conditions of the upper respiratory tract it should be one of the main remedies.

In cases of heart-disease in which there are nightly paroxysms of an intense feeling of oppression in the chest, with spasm of the bronchial tubes, suffocation, dyspnea, and an incessant, dry, metallic cough, one grain of calcium iodized every fifteen minutes usually relieves by the time the third dose is taken. The remedy does not influence the heart lesion either favorably or unfavorably.

In the night coughs of tuberculosis it is an invaluable remedy; two or three one-grain doses repeated at half-hour intervals just before bedtime will usually cause the patient to rest well until between three or four o'clock in the morning, when a few more doses repeated in the same manner will bring him comfortably through the night. It lessens hectic fever, and prevents night-sweats. It may not, however, check or retard the course of the disease when it has gone to this extent, but in phthisis generally its efficiency is practically proven.

In the coughs ascribed to irritation of the uterus, ovaries or stomach, it gives relief. In whooping-cough in full dosage, one tablet after meals, it has proven an excellent remedy. Elimination should be stimulated in all these instances. In this connection attention may be well called to the undoubted benefit derived from the use of calcium iodized in many cases of an autotoxemic character. When the stomach and intestinal walls are flabby, catarrhal and lacking in tone, the administration (after a thorough eliminative course of calomel and podophyllin, gr. 1-6 each every two hours for a day or two) will bring about a marked change for the better.

Another point worthy of consideration here is the value of calcium iodized in all throat affections causing disturbances of the voice. Singers' sore throat, "clergyman's voice," etc., will one and all be speedily benefited by Calcidin and strychnine arsenate.

For the irritative, hacking cough that frequently attends organic affections of the heart, exophthalmic goiter, etc., Calcidin is an

effective palliative, affording prompt relief and preventing the use of objectionable narcotics. The persistent daily use of small doses —gr. 1—of this remedy by corpulent persons has resulted in a remarkable loss of fat, that commences after two or three months and progresses with a rapidity that usually sends the patient to her adviser in a panic. No real harm results, and the discontinuance of the remedy checks the emaciation if too rapid.

A patient is subject to attacks of very severe gastric cramps, due to fermentation and the production of an intensely irritant acid. This is relieved by large doses of soda—a heaping teaspoonful or more. Attacked thus while on a railway journey, he swallowed the only remedy at hand, two grains of Calcidin, with instantaneous relief. Many times since then this remedy has afforded similar relief. Gastric fermentation has been invariably extinguished by Calcidin, the moment it reached the stomach.

Commencing acute coryzas usually stop if a few grains of Calcidin are given, or on the inhalation of formalin fumes.

To retain the full remedial virtues of this active agent it should be protected from light, air and moisture. If the color has faded to a grayish or white it should be discarded for fresh supplies.

From the foregoing it becomes evident that in calcium iodized the practician has:

1. An almost specific remedy for that most distressing malady, membranous croup.

2. An efficient and reliable agent in most bronchial affections, even, through its alterative influence, in reflex conditions, voice disturbances, etc.

3. In dyspnea (whether due to affections of the bronchi and lungs or to cardiac disturbances) it proves of prompt service—as it does also in asthma.

4. It rapidly causes a reduction and gradual absorption of fibroids of the uterus.

5. It is possibly the most rapid and certain remedy for coryza.

6. It enables the doctor to administer iodine in larger quantities for a longer time without causing unpleasant systemic effects.

7. In goiter and all glandular diseases, Calcidin with nuclein will prove probably the most efficient of all known remedies.

The conditions calling for the use of iodine are often the ones which also require the lime salts; the converse is also true; therefore we have in calcium iodized a form of medication which gives not only the most perfect iodine effect, but does it without causing

the slightest sign of iodism and provides at the same time, in a most acceptable form, the lime salt which is necessary.

CALCIUM SULPHIDE

Standard granules—gr. 1-6, Gm. 0.01; gr. 1-2, Gm. 0.03.

When Ringer's Therapeutics first appeared, the medical profession was startled to find very small doses of some remedies recommended, which caused the epithet of "homeopathist" to be hurled against the author. At that time even the slight innovation of dividing the ordinary daily dose into ten or twenty portions instead of three was sufficient to arouse doubt as to a doctor's orthodoxy. One of the most suspicious articles he recommended was calcium sulphide, in doses of gr. 1-10 every hour. In the form of potassium sulphuret the former Dispensatories contained long articles advocating the use of this, or of sulphurous acid, but not a word on calcium sulphide. Little impression, however, was made upon the practice of the profession; the drug was neglected, and consigned to the boneyard of discarded remedies, retaining a place in attenuated form with the homeopathists under the name of "hepar sulph."—a sort of "in memoriam," as it were, but one which has been of real value, as you shall see.

Ringer's reintroduction of the drug was followed by some desultory trials, but its use gradually died out, with the single exception of its employment as an abortive of boils, for which some insisted strongly that it was good; while others, equally as able observers, strenuously avowed it to be good for nothing. It has since been fairly demonstrated that their failure was due to the difficulty of obtaining the salt in a fit condition for administration, and to the very small doses given; not taking into consideration the fact that this preparation is variable (always weaker rather than stronger) and that variable preparations of this class, more than all others of which it is likewise true, *must be pushed* (increased as to amount given each time as well as to frequency of administration) until effect—to dose enough!

The sulphide of the shops consists of a mixture, in varying proportions, of calcium sulphide, calcium hyposulphate and the true calcium monosulphide, the latter constantly decreasing in relative proportion as it decomposes in the presence of the bottle-contained air. So that, as in many other instances and from the same or a similar cause, the modicum used on the doctor's prescription is practically inert. The same is also true of compressed tablets

and particularly so of tablet triturates. According to Shaller, it is an unusually good specimen that contains 30 percent of the sulphide; from that to nothing, usually practically nothing, being the points between which different preparations vary.

During the preparation of this study I have bought in the open market and had carefully tested many samples of calcium sulphide, with results as follows:

The highest test from bottles of the powder in drugstores was 9 percent; gelatin coated pills from socalled standard manufacturers, highest, 13 percent; tablets, compressed (one firm only) 60 percent; tablet triturates, 30 percent; other tablets listed, 36 to 40 percent; alkaloidal granules, 65 percent.

Calcium sulphide begins to decompose the moment it leaves the utensils of manufacture, the rapidity depending upon the amount of nonsaturated air with which it comes in contact.

The oxygen in a well-filled, tightly-corked bottle of calcium sulphide powder once good, or of ordinary tablets, never really good, from the time the process of manufacture is begun and always (especially when uncoated) growing poorer, is sufficient to render the top layer inert, and occasional opening to use will do the rest. Only when the strictly fresh sulphide is rightly made into a properly-protected but readily-disintegrating pill or granule can the full strength of this valuable agent be retained, and without this it is worthless. Hence, the varying opinions as to the therapeutic value of this preparation. So difficult is this pharmacal problem that some honest manufacturers have stricken this article from their lists, while from most of the remaining pill and tablet preparations on the shelves in the shops scarcely a trace of the distinctive odor is to be detected when the granules are broken open. A bottle containing calcium sulphide granules or tablets that are right emits no (or but slight) odor on opening, but a taste of the crushed granules at once reveals what they are. The stronger the characteristic taste the better and more reliable the preparation. The odor is not an indication of activity, some tablets that smelled strongly showing on analysis a low percentage of sulphide. Probably the odor is due principally to free sulphydric acid.

Calcium sulphide is prepared by passing a current of sulphureted hydrogen over lime, by the action of carbonate of iron or carbon oxide on calcium sulphate, or by decomposing lime with sulphide of carbon (Van Renterghem). It is a grayish white, amorphous powder with a disagreeable but characteristic odor. It is alkaline. After being exposed to the sun it possesses the property of remain-

ing luminous in the darkness; which has given it the name of "Canton phosphorus." This quality has been utilized in the manufacture of match-boxes, which are covered with a paint containing the substance. Boiling water decomposes calcium sulphide into calcium hydrate and sulphydrate. In cold water the carbonic acid sets free the sulphureted hydrogen, leaving calcium carbonate. The weakest mineral acids likewise decompose it.

If taken into the stomach during the period of acid digestion, the sulphide is decomposed to a greater or less extent, setting free the sulphureted hydrogen, part of which may be ejected in eructations in which the gas is easily recognized; of the residue, the resultant sulphurous acid is absorbed as well as the undecomposed portion; both are good, for both are active, but the undecomposed product is most desirable. Absorbed, it is broken up by the body, the surplus appearing as sulphydric acid eliminated by the lungs and skin, while the urine contains an excess of sulphates. It will thus be seen that the best results are obtained from the exhibition of calcium sulphide when the stomach content is alkaline or after it has been made alkaline, in which case its activity practically all passes into the blood and other circulating fluids to permeate, disinfect and clean up the workshop of every living cell—a veritable systemic antiseptic, a regular house-cleaner of the most desirable character.

In 1824 Woehler demonstrated that the sulphides are oxygenated in the body, but if the dose ingested is very large, part passes into the urine in the form of sulphide, which blackens the salts of lead. After toxic doses of metallic sulphides, Woehler and Orfila showed in the urine the presence of part of the salt as unmodified sulphide, besides a quantity of sulphates. Considerable quantities of the gas may be disengaged in the stomach without causing any deleterious action on the red blood cells; but if taken in through the lungs, sulphureted hydrogen unites with the hemoglobin, reducing it to methemoglobin; and this union once formed it is exceedingly difficult to break.

Respired in quantity it has caused death from rapidly-induced asphyxia; this has led to timidity in the use of the sulphides, preventing the demonstration of their therapeutic possibilities. But in gonorrhea calcium sulphide of the best quality has been given with impunity in doses ascending to fifty grains in twenty-four hours, and with marvelous curative effect; while children with diphtheria have taken two grains every two hours for days, with benefit and no harm. It has been injected intravenously with impunity. Here the acid reaches the lungs after passing the right heart, and is eliminated into

the atmosphere with the carbonic acid, the left heart receiving very little. But this, carried through the circulation, slightly stimulates the sweat glands (Rabuteau).

During its elimination by these various routes, the sulphide of calcium exerts an action on the respiratory mucosa, whose secretion is stimulated and expectoration loosened; on the sweat glands, whose excretion is likewise augmented; on the kidneys, producing diuresis by the sulphydric acid and the sulphates; and in general an increased activity of the circulation, possibly some fever and an increase of the appetite (Rabuteau).

Shaller says that the toxins produced by the bacteria of various zymotic diseases are neutralized by the presence of sulphureted hydrogen in the blood; or the white blood corpuscles are stimulated to unusual vigor and their phagocytic powers greatly increased. But it has seemed to the writer that the phenomena following saturation by the sulphides is better explained by the hypothesis that this renders the continued life and activity of these organisms in the saturated body impossible—either killing or inhibiting them. Whether this action is exerted on some microorganisms only, or upon all forms, is uncertain. The cessation of suppuration coinciding with saturation, indicates that all ordinary pyogenic bacteria are probably destroyed by the sulphides. In any event its control over mumps, scarlatina, measles, smallpox, whooping-cough, etc., is beyond question.

Tissot says: "Calcium sulphide is a harmless internal antiseptic of great value. This has been established beyond any doubt by clinical and bacteriological experimentation. This antiseptic power of calcium sulphide constitutes it the remedy in all infections, but more so in all anginas, both primary and symptomatic. This antiseptic property of calcium sulphide is not the only virtue it possesses, for it also allays pain and cures inflammations more quickly than any other agent. On what does this action depend?

"I believe myself to have been the first to point out the turgescence and humidity of the mucous membranes when under the influence of calcium sulphide. Pale and dry surfaces such as we see in many cases of diphtheria become red and moist. This agent, therefore, produces hyperemia and hypersecretion of diseased mucous membranes. And this fact is of great importance, for it explains perfectly, thanks to the labors of August Bier, the very remarkable properties of this great remedial agent reintroduced into therapeutics by one of our own school (dosimetry), the late venerable Dr. Fontaine of Bar-sur-Seine.

"What, then, are the results of the hyperemia superinduced by calcium sulphide? The answer is that this hyperemia allays the pain, kills or weakens the bacteria, stimulates the absorption of the exudates, exerts a dissolving action, and stimulates nutrition.

"Let us examine each one of these points:

"1. 'Hyperemia produced by calcium sulphide allays pain.' Many a time in treating painful sore throats I saw the pain disappearing by the simple administration of calcium sulphide without any other medicament. This fact was observed too often that one could deny the anesthetic action to calcium sulphide. This, moreover, is in conformity with experimental data. Ritter for instance demonstrated that serous infiltration diminishes nervous sensibility. On this fact is founded the anesthesia by Schleich's infiltration. So also clinical experience demonstrates that the pain of dental periostitis ceases when tumefaction appears. Lastly, we know that the heat of warm poultices checks the pain of inflammation.

"2. 'Hyperemia, hence also calcium sulphide, kills or weakens the bacteria.' Under the influence of venous stasis tissues infected by staphylococci, streptococci and colon bacilli rid themselves rapidly of these pathogenic agents which war against the protective powers of the blood, and the blood-plasma becomes absolutely sterile, showing clearly that all the microorganisms have been annihilated. Venous stasis renders painless those articulations into which the gonococci have penetrated. It also annihilates other inducers of rheumatism. Neither does the tubercle bacillus resist this beneficent action, while the bacillus of Eberth, the micrococcus of erysipelas and that of pneumonia are in the same case.

"According to Hamburger this action is due to a certain modification of the blood, the same becoming richer in carbonic acid, while at the same time its toxicity is augmented. Now, it is a matter of fact that the blood is in better condition to defend itself against pathogenic organisms, the Loeffler bacillus included, the more alkaline it is relative to normal. Heat aids in maintaining this high alkalinity. This justifies the choice of the calcium base in order to render the hydrogen sulphide, which is the active principle of calcium sulphide, more transportable and utilizable. However, this action of carbonic acid (itself, too, a bactericide) and the increased alkalinity of the blood are not the only factors here concerned, but phagocytosis as well as the cytolysines evidently also play their parts.

"Summing up, we may say that we find that hyperemia is a bacteriocidic agent of the very first order.

"3. 'Hyperemia, hence also calcium sulphide, stimulates the absorption of the exudates of bacterial products.' This absorption is accomplished not by the lymphatics but by the blood-vessels, and hyperemia bringing the blood into long-continued contact with the products of bacteria cannot but accomplish a great deal of good by unfailingly and completely destroying these products. This destruction *in loco* diminishes the general phenomena. If the absorption is augmented, the action is not injurious because it remains local, the battle being fought in the hyperemic tissues and the diffusion of toxins to the rest of the body is less intense; the heart, the liver and the kidneys are exposed to a less quantity of toxins than if hyperemia had not intervened.

"This increased absorption becomes directly valuable in the buccal, laryngeal and pharyngeal mucosæ. The hydrogen set free in the mouth by the action of the saliva on the monosulphide of calcium is at once absorbed and appropriated by the diseased tissues, and the antiseptic action of hydrogen sulphide is so much more pronounced.

"4. 'Hyperemia has a dissolvent action.' Billroth writes, on this subject, as follows: 'It is well known that infiltrated and inflamed connective tissue may completely disappear by absorption. It is also known that cartilage and even bone may in the course of inflammation be transformed into soluble substances, and that it is only tendon, hair and nails that are refractory to such a dissolution.' This action is due to certain cells which emigrate from the blood into the tissues; they transform the tissues into a gelatinoid mass. These digestant cells are the leucocytes which act through their enzymes. Buchner demonstrated the part which the leucocytes play in the phenomena of assimilation and disassimilation. The enzymes of the leucocytes dissolve all that which does not belong to the organism, all that which is foreign to it. The body takes from that debris whatever is subservient to it and rejects the rest or puts it away in store in such a way as to render it inoffensive.

"The cytolysis (power of dissolving cells) of the leucocytes sets free their enzymes and favors at the same time the warfare on the microbes. Hence the beneficent action of the cytolytic x-rays in experimental peritonitis, which action extends to the microbes, of which they are the best destroyers.

"5. 'Hyperemia, and therefore calcium sulphide, stimulates nutrition.' Hyperemia is the cause of functional hypertrophy. It not rarely happens that a member of the body grows larger and stronger in consequence of a venous thrombosis which merely

hinders but does not completely obstruct the blood-current. Other facts point in the same direction. Thus the nails and hair grow more rapidly in the summer, when the heat of the season brings the blood more to the surface of the body than they do in the colder weather of the winter. So also is the epithelium through hyperemia. In venous stasis of the lungs the alveoli fill up with desquamated epithelium but which is immediately replaced. So, too, are the edges of an ulcer hypertrophied because of this same hyperemia. Then, again, when we transplant the spur of a cock into his comb the spur grows immoderately because of the hyperemia of the comb causing it to become hypertrophic. Venous stasis of a pathologic nature in the various viscera brings on hypertrophy of the elements of those viscera.

"It is, I think, needless to multiply these examples. It is correct to say that the blood which is both nourisher and defender would not defend without overnourishing, i. e., without inducing a condition of hypertrophy.

"Production of antisepsis and hyperemia, these are the two valuable properties of calcium sulphide which complement each other most admirably. In one phase it destroys or more or less paralyzes the noxious elements, while in the other it acts beneficially as anesthetic, absorbent, dissolvent, and hypertrophier by hyperemia."

The remarkable power exerted over diphtheria by calcium sulphide is a discovery which the world owes to Fontaine, of Bar-sur-Seine, whose first paper appeared in 1875. Increasing the bronchial and cutaneous excretions, it aids in eliminating the toxin. But the principal effect for which it is given is that of a parasiticide, as which it has no equal when applied locally. Fontaine preferred the lime salt to that of potassium or soda, because the former also supplied an element needed for repairing the damage inflicted by the disease. Possibly the loose combination is more readily broken up, hence more energetic.

The earlier reports were favorable, but in desperate or malignant cases the remedy failed, as it was still given timidly in insufficient doses. But this fear was subsiding; and we find Ringer prescribing calcium sulphide in doses from gr. 1-6 up to forty times this quantity, many times a day, in anthrax, furunculosis, scrofulous ulcers, and for purulent, ichorous and sanious wounds. Fock also found it useful in acute mammary abscesses.

Tissot employed calcium sulphide in a series of 137 cases of diphtheria, all confirmed by bacteriologic investigation that showed

the presence of Loeffler's bacilli. Ten died, the rest recovered. Why did these ten die?

Five were brought in for treatment in such extremes that tracheotomy was imperative. The other five also all died within twenty-four hours of the beginning of treatment. Evidently these had received a fatal dose of toxin before treatment was instituted. The sulphide is not in any sense an antidote or an antitoxic. Examinations made by Tissot showed the presence of the bacilli in the exudate, but they were motionless. This explains the function of the sulphide—it is a germicide. But with every bacillus dead, the child may have absorbed a lethal dose of the toxin.

We know that even antitoxin will not save life in this condition; in fact, its value diminishes with every day of the disease, so that after the fourth day it is practically useless—and some of these cases were first seen on the thirteenth day. The fact that the bacilli are present in the exudate and the toxin there generated is absorbed thence into the blood, vindicates the writer, who has for many years insisted on the necessity of thoroughly efficient local antisepsis The marked immediate relief, even from a moribund state, that follows such cleansing of the nasal tract in diphtheria, leads us to look upon this as the remedy for these advanced cases where neither antitoxin nor sulphide will save life—this, and the use of strychnine freely to uphold the weakening vitality.

It will be seen therefore that neither of these four chief remedies replaces the other, or is to be compared with the others. Antitoxin neutralizes the toxin in the blood, and hurries the immunizing forces into action. Local antisepsis removes the bacillus-bearing membranes and stops the formation and absorption of toxin. Calcium sulphide kills the bacilli. Strychnine sustains the vitality.

To advocate the exclusive use of either is silly.

Chaussier had employed potassium sulphide for croup and diphtheria as early as 1808, and Ribes in 1818; but they had dropped it on account of the difficulty in administering it in potions to children; and it was not till modern pharmacy had evolved the granule that the remedy was made available.

While in diphtheria calcium sulphide is given as the dominant or leading remedy, the variants or adjuvants are by no means unimportant. Fever demands aconitine, digitalin; periodicity calls for quinine arsenate or hydroferrocyanate; emetics may promote the loosening of false membranes; strychnine restores the normal tone (Van Renterghem); and antitoxin should not be forgotten, though rarely needed.

Fontaine also urged calcium sulphide for whooping-cough, in which he has been followed by many. Droixhe at first gave the sulphide only in the second period, but later he gave it from the first, and esteemed it equal in efficacy in this malady as in diphtheria. Shaller has given it continuously for three or four weeks, always with marked reduction in the number and frequency of the paroxysms, without anemia resulting.

Coleman has obtained equal success, and claims that even in the incubation stage this disease may be aborted by saturation with calcium sulphide and the conjoint use of atropine to full effect. Since it is now admitted that this disease is due to microorganisms, and that during this period they are actively at work, it seems perfectly reasonable to suppose that they may be effectively combated then, when their numbers are small. Coleman has taken children who were not immune, saturated them with these remedies, and exposed them to this most infectious of all ailments. These children did not contract the malady then, and when exposed during subsequent epidemics proved to be immune. With all of this, from our own experience we most heartily concur.

The results obtained in these two affections encouraged trial of the sulphide in other infections. Castro tried it in smallpox. His rules are:

1. Begin treatment as soon as the malady is suspected. 2. Saturate the organism with the parasiticide. 3. Keep up the saturation until certain of the effect. 4. Even if the eruption has appeared it may be made to retrograde so that vesiculation does not occur. 5. Pustulation under way, the sulphide may still prevent complications, destroy the odor, abate considerably the fever, and attenuate the gravity of the attack in hastening desiccation. 6. The disagreeable odor of the sulphide and the necessity of giving it in numerous small doses renders the use of granules advisable, which must be known to be active if a correct judgment as to its value is to be made. 7. The intensity of the administration should be commensurate with the effects required by the nature of the case.

Castro also applied this remedy in this manner in treating roseola and erysipelas.

Van Renterghem employed the sulphide in four cases of scarlet fever, two anginous, saving all, and that in a very short time and with a brief convalescence.

Shaller says that measles, whooping-cough, scarlet fever, smallpox, diphtheria and erysipelas are all more easily controlled and freer from sequels when this remedy is used. He gives it through-

out the course, adding aconitine for fever, caffeine for threatened collapse or heart failure, strychnine for paralysis. If the throat is inflamed he gives the sulphide in solution, in severe cases every fifteen minutes, so that the solution almost constantly bathes the infected surface.

Many physicians have employed calcium sulphide in smallpox during the last epidemic in the west, and generally with good results. Given early to saturation, most cases seem to be abortive and the secondary suppuration and its fever are wanting. It is also a markedly reliable preventive or modifier in exposed cases but must be given early and in large doses. It should not be given to persons who are just vaccinated as it may check the development of normal vaccinia.

In respiratory affections Van Renterghem recommended calcium sulphide as an expectorant, in the dry coughs of commencing catarrhs; in phthisis; to increase secretion and facilitate expectoration. Shaller praises it for tough, scanty sputa in measles and pertussis with distressing cough, in chronic lung diseases where the sputa is putrid. Aulde advised this remedy to abort a commencing coryza. It has been suggested that if other microorganisms can not live in the human body when saturated with it, why should the tubercle bacillus? The question has not been settled, but is well worth consideration.

In acute gonorrhea there is no remedy, not even copaiba, which will so surely and so promptly stop the discharge; and unlike the time-honored but useless balsam, and to the great relief of the patient, the discharge does not return the moment the remedy is discontinued. The doses must be large but a permanent cure may be usually achieved. One physician reports unvarying success from doses up to fifty grains each twenty-four hours. It is the most reliable remedy in chronic gonorrhea. The writer has never known any remedy to be of benefit in gonorrheal "rheumatism," except the sulphides of calcium and arsenic; and these have not as yet failed to cure every case of this malady brought to his notice.

In various skin diseases calcium sulphide has been used locally, forming an ingredient of the famous solution of Vleminckx. In Alaska it has been found that the voracious mosquitoes will not attack a man whose skin is covered with a solution of this remedy. In the treatment of mountain or tick fever in the northwest, favorable reports have been made of this remedy.

This brings us to the question of the use of calcium sulphide as a prophylactic in malaria and in yellow fever—both transmitted

to man through the bites of mosquitoes. In the experiments made in Cuba it was found that the insects would not bite some persons at all, and that others at times were not attacked. The reason was not ascertained. Persons who drink artesian water, which is often charged with sulphides, are not affected by malaria. It seems worth trial, to see if mosquitoes will attack men who are saturated with this agent so that their skins exhale it; as if so, the problem of immunity to those whose duty requires their exposure at night may be simplified.

Van Renterghem advises that calcium sulphide be given, even to infants of the most tender age, in granules containing gr. 1-6 every quarter hour in acute cases; to adults two or more granules; until saturation is denoted by the odor of the drug appearing on the breath *or the skin.* The eructation of sulphureted hydrogen is less certain as the acid gastric juice will decompose the salt and disengage the gas even when a single dose has been given. If the drug is pushed too rapidly it may cause nausea and this has been taken to indicate saturation; but is rather an indication for smaller doses.

After saturation has been secured the doses need not be given so frequently, but just enough to keep up this effect as long as it is deemed requisite. In infectious diseases it is well to sustain saturation for one week; in tuberculosis for two or more weeks; in general, till the danger has ceased.

How much is required to produce saturation? The dose varies. Fontaine gave 20 granules to a child a year old, 30 to one of 22 months, 60 to adults, within twenty-four hours. Castro gave 60 to 90 granules to adults in the same time. As a prophylactic five granules may be given daily to infants, ten to adults—just "dose enough" is right. Fontaine says that when calcium sulphide was administered to all the children as a prophylactic, during an epidemic of diphtheria, he was frequently called to see adults ill with that malady when the children in the house, taking the sulphide, were immune. The epidemic really ceased only when the use of this prophylactic had become general.

Externally, solutions of one part to ten of water may be applied; the skin to be washed soon to avoid undue irritation. A better and more enduring application is a solution in glycerin and water.

The solutions for use must be freshly prepared each day, as they quickly decompose. Glass spoons should be used for dispensing, as silver is blackened by it. Shaller says that persons who swallow the granules do not tire of the medicine as soon as those who take it in solution; that is also our experience. If the eructa-

tions are disagreeable the remedy should not be taken just after meals or during continuance of acid digestion.

In some cases where there is intense acidity calcium sulphide will not be tolerated by the patient, as each dose will cause nausea or even vomiting. This annoying condition can be promptly controlled by exhibiting two grains of vegetable charcoal ten or fifteen minutes before the calcium sulphide. The writer has found that results are more speedy and pronounced when these remedies are given together in this manner.

Experience has amply proven that the small dose at frequent intervals is the most effective. The ordinary compressed tablets containing one-half and one grain and coated or uncoated are practically useless; they pass from the stomach into the intestine, where no chemical change takes place. To bring a patient promptly under the effect of this drug two or four granules, gr. 1-6, should be given hourly or half-hourly and one granule (gr. 1-6) will usually prove quite as efficient. The secret of success is to saturate the system quickly and then to maintain this condition with smaller doses given at longer intervals. The calcium sulphide patient usually calls also for eliminatives and the tonic arsenates.

It will, therefore, be seen that to have a good preparation is most essential and that even this may be given wrongly. A good preparation chemically broken up in the stomach and given to "dose enough" will produce results most desirable and satisfactory.

The difficulty in securing and handling pharmacally this drug is great. One specimen in our laboratory tested up to 98 percent; but had scarcely any odor. This specimen proved simply unworkable into tablets or granules and had to be discarded. Is the odor due to the salt or to uncombined acid? The latter seems probably true.

E. D. Ault reports two cases of urticaria following saturation with calcium sulphide for membranous sore throat, probably diphtheritic.

L. A. Merriam, of Nebraska, says: "Calcium sulphide is of value in all cases where there is formation of pus; also in mucous discharges, cough, gonorrhea, leucorrhea, excessive granulation, festers, furuncles, pimples, pustules and skin affections with yellowish scabs, purulent diarrhea, dysentery and pus-like slimy discharges from the bowels."

The late Professor E. L. Clifford employed calcium sulphide in the treatment of pyorrhea alveolaris, and with remarkable success. He began by clearing the alimentary canal with saline

laxative, disinfecting with sulphocarbolates, and put an end to pus-formation by saturation with the sulphide. This method is being tested at large by competent experimentors, and so far with encouraging results.

CAMPHOR MONOBROMIDE

Standard granule—gr. 1-6, Gm. .01. Tablet, gr. j, Gm. .06.

Sollmann says the stimulation of camphor is exerted mainly on the medulla. He sums the action thus: Stimulation of the central nervous system followed by paralysis from large doses; in mammals mainly acting on the vasomotor center. Stimulation of the cardiac muscle. Locally stimulation and paralysis of the sensory nerve ends; also stimulation of the nerves conveying the sensation of cold (by menthol). Peripheral depression of vascular tone. Mild antisepsis as with the volatile oils. A curare action on striped muscle.

The action on the circulation is complicated: The mammal heart is not stimulated by small or by medium doses. Larger doses prevent delirium cordis from electric stimulation, and revive the heart poisoned by potassium; still larger doses depress the heart directly. Vascular pressure usually falls, from direct depression of the arterial muscle. Camphor is also a quite efficient intestinal antiseptic, the urinary combined sulphates being lessened by it. Absorption is variable, usually rapid, from its volatility. The camphors are converted in the body into hydroxyls unless they already contain this radicle (Fromm and Hildebrand).

Camphor monobromide is obtained by the direct action of bromine on camphor. It crystallizes in monoclinic prisms, little soluble in water, sparingly in cold and freely in hot alcohol, easily in ether, chloroform, oils, or benzole. The odor resembles that of camphor.

The contradictory reports on this salt appear to show that it acts as camphor and as a bromide, not as a new body. The bromine is not excreted by the kidneys (Liebreich). It reduces the pulse, the respiration and the temperature (Bourneville and Lawson). It induces clonic spasms of the feet, with maximal dilatation of the pupils during the spasms; hallucinations, insomnia and emaciation when its use is continued long (Nothnagel). Large doses cause poisoning with the same results as camphor.

Cushny says it acts as camphor, the bromine having no effect. Wood says that it causes violent convulsions, with muscular weak-

ness almost to the point of paralysis; small doses lowering the temperature after an evanescent rise, with great diminution in the rate of the respiration and of the heart, with occasional periods of hurry in each. It induces stupor ending in death. The vessels of the eye and ear are contracted. Doses of 45 grains caused tremblings, slow pulse, and coma lasting six hours.

Hare found it caused Cheyne-Stokes respiration, the pulse at first rapid and then becoming slow and weak. Death may occur either in coma or in convulsions.

Van Renterghem experimented on himself with camphor monobromide as follows: The first day he took two granules, gr. 1-6 each, every hour for ten doses, allowing the granules to dissolve in the mouth. The local action on the buccal mucosa was limited to a sensation of fresh warmth, with salivary and mucous secretion. Next day he took five granules every hour for eight doses. On neither day was there any special symptom that could be charged to the remedy. The appetite was good, the sleep if anything more than usually profound. The third day he took fifteen granules hourly for four doses. Fifteen minutes after the fourth dose he felt a sense of warmth in the face; the forehead, face and neck covered with sweat, the lips pale, with a sense of vertigo and as if being raised from the earth. The pulse was unaffected, the respirations calm. Dinner was then ready, but he could not swallow a morsel. This state endured an hour and subsided slowly. Although able to attend to business it was not till next day, after a good night, that he felt himself as usual and the gastric derangement had subsided. Under the influence of the massive doses his temper was irritable.

Burggraeve, taking this agent during a cold in the head, observed after a dose of four granules a diminution of the tactile sense of the pharyngolaryngeal mucosa. According to him, camphor monobromide realizes the ancient saying of camphor: "Camphor dissolves spasms."

Van Renterghem concluded from his trials that in light doses, of two to five granules hourly, this drug is harmless to a well man; while in doses of gr. 2 1-2 hourly, it deranges the stomach and causes intoxication.

Therapeutics.—Deneffe employed camphor monobromide in delirium tremens, giving 3 to 4 Grams. Hamilton gave it with benefit in chordee; Gallard in chorea; Vulpian and Potain in hysteric spasms, palpitations, dyspnea and spermatorrhea; Charcot and Bourneville in epilepsy; Desnos in prosopalgia; Lannelongue

in painful affections of the bladder; Rosenthal in nervous palpitations and excessive irritability of the bladder. Veterinarians have reported success with it in treating sexual manifestations in the horse, dog, cat and bull.

Sollmann recommends camphor in collapse, syncope, adynamic fevers, cardiac failure, etc., given hypodermically as camphorated oil, 1-2 c.c. every fifteen minutes for four doses. The action is inconstant. As a diaphoretic in colds, camphor acts well by dilating the vessels of the skin.

Landrin found that moderate doses prevented irritation of the urinary apparatus from the absorption of cantharidin from blisters.

Van Renterghem recommends camphor monobromide in the dryness of the tissues in typhus and cholera; in all inflammations of the respiratory, digestive and genitourinary ways; in all cases with tendency to exudation or the formation of false membrane; in irritations of the larynx and œsophagus; in asthma and emphysema, spasmodic and convulsive coughs, whooping-cough; certain cardiac palpitations, nervous or symptomatic of organic lesions; for hyperemias in general and affections of the cerebral nervous centers of congestive form or due to stimulants; for urethral erethism, the debut of gonorrheas with chordee. He considers it the best sedative of the genital system, for nymphomania, hysteria, pollutions and priapism.

Berger pronounced it of value only in nervous palpitations and in irritability of the genitourinary organs. Rosenthal obtained good results in hysteric and nervous headaches. It has been suggested for paralysis agitans, and Liebreich deemed it effective in hysteroepilepsy.

Wood found it useful in hysteric excitement, sexual irritation and spermatorrhea, but of little value in delirium tremens; but Hare advises it in the latter when the gastric mucous membrane is depressed and there are violent twitchings. For pain, Hare advised this remedy in connection with others, as in lumbago; also as a hypnotic in hysteria, for whooping-cough, chorea, epilepsy and *petit mal*, and for the nervous depression and pains of influenza. Like crude camphor, the monobromide warms and in overdoses irritates the stomach.

Bourneville recommended it in vertiginous epilepsy, but not in the ordinary forms.

Laura credits this compound with remarkable properties. "It is eminently sedative, modifying rapidly and in a sufficiently stable manner the state of the nerve centers, principally those show-

ing morbid exaggeration of the nervous reflexes. The sedative power is exercised upon the encephalon, the spinal cord, or both. Besides, this remedy may exert an influence in some manner elective over some special part or apparatus in the animal economy.

"Camphor monobromide is specific in all exaltative or erethetic states of the encephalon; alone, as in primary nervous encephalopathies; associated with other modifiers of the nerves or of the sanguine crasis, when there are complications or particular states offering the indications. It is applicable in nervous cerebralgias, central neuralgias, insomnia, and other morbid manifestations due to an exaggerated excitability of the encephalon.

"This bromide renders signal services, not only in the dolorous neuropathies, but still more manifestly in the spasmodic forms dependent upon irritative nervous states and excessive irritability of the brain or cord. It is therefore very useful in chorea, spasmodic hysteropathy and in epilepsy properly so termed, provided these are not dependent upon certain irremediable states and pathologic processes.

"All are aware that epilepsy is often obstinate and rebellious, and this pest is a peril not only to the patient but to his family and to society. Against epilepsy the tradition-governed school and its numerous adepts, with the authority of hundreds of masters, famous and vaunted, ordain the bromide of potassium; or, less frequently, the bromide of sodium. Of late they have advised, not without reason, the simultaneous employment of the bromides of potassium, sodium and ammonium. If chloroanemia is present also, we advise the use of iron bromide.

"We can scarcely count the maladies against which we employ the bromides, through exaggerated admiration or a false estimate of their powers. They have been wrongly vaunted in diseases scarcely to be ameliorated and altogether incurable. Such intemperance is as compromising to the dignity of the art as it is injurious to the patient, whose condition is thereby aggravated.

"In epilepsy the bromides render services which we are far from denying, when given in appropriate time and manner; while they are useless and often dangerous when given, as is usually the case, in doses excessive and too long continued. Many epileptics consult us with whom the abuse of the bromides, continued for months and years, has engendered the greatest ills, ruined the vitality of the stomach and the brain, denatured in the bosom of the nervous cellule the intimate nutrition and the function itself; to the point that in presence of loss of memory and of spirit, with moral and

physical depression, it is difficult to say what is due to the disease and what to the remedy. Things have gone so far that the clinical formula 'epilepsy' is answered with the therapeutic formula, 'potassium bromide;' reducing to the simplicity of an algebraic formula matters most frequently of a nature complex and variable.

"It is necessary to know that epilepsy presents itself with one person in a form very different from that under which it appears with another. Its origins, periods, concomitants, complications, hereditary antecedents, sanguine crases, diverse dyscrasias and the functionation of the gastric apparatus, are the coefficients of the disease or of its manifestations, constituting a clinical grouping and pointing to very variable therapeutic indications; obliging the practician to choose modifiers, hygienic, moral and medicamentous, after Burggraeve's true and just law of the Dominant and the Variant. This law is universal in the treatment of every malady.

"We will here say that atropine is the sovereign remedy for epileptic convulsions and other forms of epilepsy, in which camphor monobromide will prove useful as an adjuvant. With this association, in essential epilepsies the cure may be obtained in some weeks, and prove durable. In chronic epilepsies where the nervous nutrition has already suffered incurable material alterations, we may yet obtain in many cases results not to be disdained; and in ordinary chronic epilepsies the paroxysms diminish in frequency and in intensity; moreover, during the atropine treatment the attacks are very often prevented.

"In secondary epilepsies the causal condition requires treatment as the first indication. In complicated cases, we must cure the complications by appropriate methods. In epilepsies with special dyscrasias, besides the general treatment the specific rational management is requisite.

"In all epilepsies we must comprehend the necessity of providing for the functional disequilibrium, and associate with the moral and hygienic therapeutics the powerful alkaloidal modifiers.

"Camphor monobromide finds its place in the treatment of all spasmodic affections of smooth muscular fiber; where hyoscyamine, morphine and even strychnine may also be of very great utility. Strychnine is a sovereign calmant of all motor or sensory neuropathies, that depend on exaltation of the nervous system through feebleness, exhaustion, insufficiency or failure of the physiologic stimulus. In these cases strychnine puts an end very speedily, and without causing any other trouble, to the painful or spasmodic neuropathic forms. It is so true in therapeutics that the result

depends on the adaptation of the particular property of each medicament to the corresponding morbid element, that one sees the dosimetric incitants become on occasion the sedatives of the nervous system, to which they give the life and the excitation necessary for the resumption of their natural rôle.

"Camphor monobromide also exercises a selective action upon the sexual organs, especially of men. This action is exerted partly through the spinal cord, which it calms, and partly by a direct action upon the sexual organs, since it can stop the spermatorrhea produced by excessive spermatic secretion, due to excessive activity of the seminal glands. This sexual sedative power of camphor was known to the ancients, who formulated the aphorism: "*Camphora per nares castrat odore mores.*" Some, however, have held that camphor is aphrodisiac."

Laura recommends the monobromide in erethism, even in the female; in nymphomania, in hysteropathy of uterine origin, in the aberrations so varied and almost unbelievable of the victim of masturbation, in excessive excitation of the clitoris; adding here hyoscyamine, atropine and even cicutine, as they may be indicated.

"Camphor monobromide finds also a legitimate employment against satyriasis and priapism, against the premature and excessive irritability and excitability of the sexual apparatus of man or woman. It should be given for spermatorrheas, central or testicular, often so obstinate as to demand surgical or mechanical measures. Pathault has obtained good results from this remedy in nocturnal pollutions; here Burggraeve advised the addition of atropine.

"In anemic complications iron and arsenic should be also employed. Well-directed hygienic and moral treatment are useful auxiliaries."

Burggraeve advised this salt in rabies, in nymphomania and in hysteria. Laura advised it in general as a substitute for potassium bromide. Charcot, Tommasi, Pathault and others preferred it to the latter, as more efficacious, in convulsions and neuralgias, "especially in epilepsy, in infantile eclampsia, chorea, hysteria, sexual erethism and the ovarian neuralgias of the hysteric" (Cantani). Bourneville found camphor monobromide specially indicated in epileptic vertigo, *petit mal*, and in the *grand mal* so fatal to the function of the brain and to the intellectual life. This remedy is also useful in palpitations of the heart and in nervous dyspnea. It is of service in cystalgia and in tenesmus of the bladder; but here the union of hyoscyamine, cicutine and strychnine is preferable.

"When administered according to dosimetric methods one is absolutely sure of avoiding the inconveniences of massive doses—dyspepsias, catarrhs, hypothermia, emaciation; and, with excessive doses, hallucinations. The dose varies with the malady, its nature, its energy, its duration and its resistance, the effects desired, the age and the very exceptional idiosyncrasies. Of the granules, each containing gr. 1-6, the daily dose may be 10 to 30, and these may be increased if desirable, with safety. Rarely should one pass 50 granules in one day."

It has been some years since Laura wrote the fine chapter on camphor monobromide, of which the foregoing is a free transcript. He did not in the least overvalue this remedy. As offering in an enhanced form all the values accruing to the use of potassium bromide, yet avoiding the vital depression following the use of this salt, and obtaining all the desirable results of the bromide medication from relatively minute doses, the monobromide of camphor is too important a remedy to be neglected.

In the development of precise therapeutics in America two remedies have arisen that were unknown to Burggraeve and Laura, each of which has notably restricted the field of camphor monobromide. The alkaloid solanine possesses in a remarkable manner the precise effects for which the bromides are employed, without depressing the vitality or interfering with digestion. A dose of gr. 1-12 equals in power about fifteen grains of potassium bromide, and the administration is much easier. It may also be employed hypodermically, and the effects are much more rapidly induced. Solanine has only to become better known to render the "big dose" bromides obsolescent.

For the entire group of erethetic maladies, spermatorrhea, impotence, feeble erections and premature ejaculations, with the inevitable melancholia and hypochondria, the local application of thymol iodide in fluid petrolatum, *chemically pure*, to the prostatic urethra, has revolutionized the treatment of this former *bête noir* of the practician. The field for camphor monobromide remains nevertheless a large one.

In many cases it seems a question if any sedative can be used, and yet there are irritative symptoms that need sedation. The combination of a calmant with a powerful restorative like camphor is admirably suited to this indication, and the monobromide of camphor has won laurels in many such instances. The insomnia of fatigue, and that of nervous exhaustion, are usefully treated by this agent in doses of seven grains at bedtime, or a grain every

quarter-hour till effect. For such conditions in children it is simply admirable. It does not usually irritate the stomach as crude camphor does; in fact, the writer's experience directly contradicts Cushny's statement, for if either ingredient is covered up, it is the camphor. In fact, in many cases, giving this salt for acute colds, the desired camphor effect has not been obtained.

As a sexual sedative it is far more reliable than camphor, which is as liable to act as an aphrodisiac as the contrary, but the monobromide has never failed to give pure and unmixed sedation of this function.

Even in irritable conditions of the stomach this remedy has not caused distress or nausea, in the small doses deemed advisable there. A granule of gr. 1-6 may be administered every five minutes for an hour or two, when a single dose of five grains would possibly cause trouble.

Children with whooping-cough take two to five grains at a dose without irritation, and here it has proved in our hands a valuable sedative for the cough, though not shortening the attack as calcium sulphide or formalin will do. Camphor monobromide does not have the injurious effect on the digestive organs, and the depressing effect on the vitality, that are sure to follow the prolonged use of potassium bromide. In fact for children and delicate females, the latter in our practice has been entirely superseded by the camphor monobromide.

If the temperature falls below normal the administration of camphor monobromide must be suspended. It is too irritating to be used hypodermically, but if this should be deemed necessary the solution in oil could be utilized, the dose being 1 1-2 grains.

CANNABIS INDICA

Standard granules—Cannabin resin, gr. 1-67, Gm. .001; cannabin tannate, gr. 1-67, Gm. .001; cannabin and atropine comp. (Cannabin, gr. 1-50; atropine sulphate, gr. 1-100.)

The use of this drug as an intoxicant, hypnotic and aphrodisiac in the East has invested it with unusual interest. Under the names of hasheesh, bhang and gunjah it fills with many races the places of opium and tobacco, and of alcohol. But though it has frequently been introduced into medical practice it has never sustained the place for which it was urged, or dislodged the more objectionable agents for which it has been proposed to substitute it.

No drug would seem better calculated to display the advantages of Alkalometry than this, because it possesses exceedingly valuable

properties, but is scarcely used on account of the uncertainty and unreliability of its preparations. But up to the present it has defied all efforts to find an active principle from which its remedial virtues can be obtained.

Merck lists cannabin, a resinoid; cannabindon, a liquid, dose m. 1-3 to 1; cannabine alkaloid, dose gr. 1 1-2 to 4; cannabine tannate, dose gr. 8 to 16, maximum daily, gr. 40; cannabinine; cannabinon, dose gr. 1-2 to 1 1-2; and an alcoholic extract, dose gr. 1-4 to 2, maximum daily gr. 5

Cushny pronounces all the above merely impure extracts. Hay reported the discovery of tetanocannabine, with effects similar to those of strychnine; but this has not been confirmed. Vignolo says cannabis contains muscarine, and traces a similarity of effect with the mushrooms used in Russia to produce pleasurable intoxication.

A good extract like Allen's gives therapeutic effects in doses of gr. 1-4 to 1-2. It is obvious that no derivative requiring doses in excess of these can be looked upon as the active principle. The extracts vary greatly, and every new sample requires testing anew. But the drug is worth it; as we hope to show.

Physiologic Action.—Brunton pronounces cannabis hypnotic and analgesic. In some it causes visions or hallucinations previous to sleep, of pleasant nature or otherwise. It is not an aphrodisiac, but gives rise to erotic dreams or hallucinations, more frequently in Asiatics than in Europeans. Sometimes it causes delirium, or tendency to active movements, sensible or erratic, rarely homicidal. In Europeans the dreams may be disagreeable. In Asia it is the custom to give other aphrodisiacs with cannabis to give the visions this coloring. The patient under its influence may talk and act apparently in a sane manner, while really not so. In some cases there is a curious loss of the sense of time and space, so that ages apparently elapse in a moment. In others the phenomenon of double consciousness is presented, the two sides of the brain appearing to act independently. Given short of hypnosis a dreamy state supervenes, the judgment being in abeyance, the imagination free. The visions and speech may show boundless extravagance, but vary with the individual. The movements may be absurd, the ideas incoherent; there may be a sense of impending danger or death, or the condition is of euphoria, comfort, well-being, self-satisfaction. Consciousness is not all lost but restraint is weakened or lost. When aroused or questioned the answers may be rational. The sense of pain is weakened or lost, that of touch lost. In some

this pleasant stage is absent and there is merely a heavy, drowsy feeling, with tinnitus, and numbness. Some experience a sense of fullness in the chest, as if it were bursting. Heaviness of the arms and legs may be felt, the head is hot and heavy, the eyes bright and shining, with dizziness, noises in the ears and pleasant anesthesia. Pressure excites a sense of burning. Rarely the drug causes maniacal attacks or convulsions. Periods of unconsciousness alternate with the foregoing, and finally deep and healthful sleep supervenes. Some say sleep is secured in only fifty percent of cases, but this is too little, in our experience.

From this sleep the patient awakes refreshed, with no headache or disturbance of the digestion—no nausea or constipation.

Cannabis affects the nervous centers like morphine, with a mixture of sedation and stimulation. The respiration may be accelerated or slowed, the action on the pulse also being irregular, first faster, then slower. The temperature may be raised or lowered as motion is or is not induced, falling as sleep comes on. The sensory nerves are benumbed, the pupils dilate. The legs especially become anesthetic. Large doses, however, slow the respiration quite uniformly. Death from cannabis is very rare; Hare says none has ever been reported.

The nutrition is not affected by the habitual use of this drug. Shoemaker says it causes mental deterioration and unfitness for work. In the East the use is said to lead to dementia or mania.

Locally cannabis is an irritant to muscular tissue, anesthesia following; but the irritation is too great to allow its use as a local anesthetic.

Cannabis increases the excretion of urine.

Therapeutics.—Cannabis covers a large field. Brunton recommended it as a hypnotic in acute and chronic mania; as an analgesic in neuralgia, migraine, etc.; to relieve spasmodic coughs; and for menorrhagia. For constant headaches, from cerebral tumors and other causes, this author recommends it. It relieves the tremors of senility and of paralysis agitans; the lightning pains of locomotor ataxia; gastralgia and enteralgia—in fact Germain Sèe pronounced it a specific for pains below the diaphragm. Even the agonies of renal and hepatic calculi are eased by cannabis, as well as those of rheumatism, gout and cancer. It relieves the delirium of softening of the brain, and a dose at bedtime puts a stop to unpleasant dreams. Taken internally it stops the itching of eczema as well as senile and many other forms of pruritus; but a caution as to the formation of a cannabis habit is here necessary.

Pains in the uterus are relieved by cannabis, while its contractions are increased and steadied; in which we may find a reason for the use of this agent in uterine hemorrhages, both menorrhagia and metrorrhagia. It relieves the headaches and checks the hemorrhages of the menopause, and in fact is vaunted as a general hemostatic.

Does it cure diabetes? Probably not, but at least it relieves the attendant cerebral irritation and the itching.

It has been praised as a remedy for asthma, whooping-cough and hay fever; for tickling in the throat, and for the cough of advanced phthisis, where it long enables us to postpone the resort to morphine.

See particularly recommended cannabis as a sedative in gastric cases with pain, acidity and flatulence; also in gastric ulcer. In pain from nerve disturbance Hare advises it; as in migraine, giving first a full dose of gelsemium and then cannabis; also in true migraine with hemianopsia which it aborts very effectively. He suggests it in paralysis agitans, spasm of the bladder, and in inorganic impotence, in headache from retinal asthenopia, in subinvolution and chronic metritis, in nervous and spasmodic dysentery, and for chordee. In acute and chronic nephritis it relieves the hematuria and the pain.

Murrell testifies to its benefits in sick headaches.

Cannabis has been used with asserted success for exophthalmic goiter.

Shoemaker advises it as a hypnotic for acute dementia from anxiety, and for melancholy; also in delirium tremens. He mentions its use in tetanus and in epilepsy.

Cannabis has been used in the treatment of opium and other habits, with some success. If the narcomania cannot be entirely cured, it is unquestionably better that the patient should substitute the cannabis habit for any opiate; but in all the cases in which the writer tried to do this he failed. The patients quite willingly added this drug habit to their other accomplishments, but there they quit.

In the latter stages of incurable phthisis, cancer and other painful affections, the greatest relief ensues from the formation of the cannabis habit. In painful affections of the heart, such as angina pectoris, the pain-relieving and muscle-steadying effects noted in uterine maladies might be duplicated.

Tissot writes: "This alkaloid is not very much used in alkalometry. It claims its place only where other hypnotic alkaloids are not tolerated. Among others it is certainly useful in the treat-

ment of gastralgias. Germain Sèe has even denominated it, "the antigastralgic *par excellence*."

"Cannabis is of the nettle kind. Cannabis sativa is diœcious. The male plants have terminal spikes, and the female plants have an inflorescence in the axillæ of the leaves. The cannabis of India has no morphological points to distinguish it from our cannabis, except that the former has a characteristically different content of resin.

"The female plant elaborates in its inflorescence, during the season the only substance used in medicine. The resin which it secretes allows its inflorescence to form itself into a greenish-brown mass which is the substance called *hashish*, also bhang, bheng, sabzi, siddhi, as synonyms.

"The amount of the resin in the hashish which comes to Europe is twenty per cent. This resin contains:

"1. A volatile alkaloid called *cannabine*.

"2. Non-volatile alkaloid called *tetanocannabine*.

"3. A brown, amorphous resin, insoluble in basic bodies; this is called *cannatine*, or *hashishine*.

"4. An essential oil called *cannabene*, which is a carbide (carburet) of hydrogen.

"5. A crystallized body also called *cannabene*.

"The tetanocannabine acts like strychnine. It is not found in any of the preparations of hashish.

"Finally the cannabinone of commerce is an amorphous, resinous, bitter mass. This is the cannabinol of English chemists.

"The commercial tannate of cannabine is very little active.

"Cannabine is poisonous in high doses, but has been very little studied.

"Indian hemp preparations act upon the brain, hence its employment as an hypnotic. They have also a local anesthetic effect on the stomach. It is also used for the same reason in plasters and collodions to destroy corns.

"For the alkaloidotherapeutist the effect of Indian hemp on the brain is of great interest.

"Morphine, hyoscine, and atropine act on the sensible and psychomotor neurons. But Indian hemp, while it also affects the sensible neurons, affects also at the same time those neurons whose complexes form the organs of the sensations of pleasure and displeasure, which accompany our actions, volitions, perceptions, sentiments, and most of our psychic actions. These sensations of pleasure and displeasure play an immense part in our lives.

The first is the optimism and the joy of life and the cheerfulness of labor, the other is the characteristic of melancholics, and of bruised hearts.

"The action of Indian hemp seems to show that there is a distinct organ for the sensation of pleasure and another for that of displeasure.

"This special action on these precise cerebral regions makes it that at the present time two hundred millions of human beings have given themselves up to hashish for the last two thousand years. The use of this seems to have come from Asia Minor, and thence it spread to the Indies and to Africa. The negroes of the Congo, the Hottentots, the Makololos and Damaras have that passion for this poison which marks the coolies of China, and the millions of Hindoos.

"Lewin gives a complete and touching picture of the pharmacological effects of hashish.

"It was often said that hashish excites first of all the genital functions. Erotic representations may indeed traverse the dreams which the smokers and eaters of hashish procure from it. At first the genital functions may be exalted, but there is no more of this during the ensuing paroxysms and at the ending of the toxic effects. Smaller doses make a person gay and at times provoke convulsive laughter.

"Stronger doses produce a delicious sensation accompanied by psychic actions. All ideas are, as it were, lit up with sunlight and leave a luminous track behind them in the brain. Every movement becomes a source of joyfulness.

"The sensation of the hashish eater is not analogous to that of the gourmand who partakes of a good dinner, or of a starveling who has found enough to eat his fill. No, he is as happy as one who gets hold of a good novel. He feels what the miser does when he counts over his treasure, what the gambler feels when chance has favored him, what the ambitious person feels who met with success.

"All the senses gain in acuteness. The auditory sense is no longer merely proportionate to what the sound waves produce. The ear hears harmonies when none have taken place. One single luminous ray becomes a bright sun, and that sun irradiates a paradise of the greatest voluptuousness.

"In this condition the eater or smoker of hashish feels that he has no body, and the notions of time and space no longer exist for him. At times somber ideas take hold of the intoxicated one. The African smokers do not sleep as others do after the sensations

described above have passed off, but are rather excited, and their talk becomes a rapid and tumultous current of words without any sense, whose phrases are short cut.

"Persons of this kind are but little agitated. A great agitation takes hold of Europeans only, who dare partake of this poison.

"These cannabists dance an infernal saraband in the room where they are. Their ideas veer about so quickly that they cannot be fixed for a single instant. Their speaking acquires an incredible volubility. European cannabists creep sometimes on all fours, and though conscious of what they are doing, they show no inclination to do otherwise. I have myself seen, some twenty years ago, two students who, after smoking hashish, abandoned themselves to the making of such exercises in the streets of a little village, which astonished their population. One of these leaped, with his feet close to each other, over a boundary stone and imagined that he cleared the Alps at a single bound. The other one strode over a puddle of water and believed he had crossed a lake. At last they went to their room and demolished a crockery pan and used the pieces as projectiles.

"Chronic cannabism produces devastations in the body and in the brain analogous to those which opium does.

(Those caused by cannabis are more disastrous to the intellect.)

"The tannate of cannabine acts in about half of the cases as a hypnotic. Its frequent side-effects are (in a dose of Gm. 0.1—0.5) vomiting, insomnia, and restlessness. (See Lewin, *Nebenwirkungen der Arzneimettel.*) Observed also were dryness of the mouth, and increase of pulsation, smallness of the blood wave, collapse, and loss of consciousness. The skin becomes insensible, and the patient feels the horrors of death. Delirium and hallucinations are frequent. One patient imagined he vomited fire, and another made suicidal attempts.

"Lastly the nervous system becomes either benumbed, or, just the contrary, it reacts with an extraordinary motility, or with convulsions.

"The frequency of these alarming symptoms makes cannabine a dangerous medicament, which when demanded should be administered dosimetrically only. This measure of precaution will not prevent frequent failures in the sense of rendering this medicament altogether null. I repeat that the employment of cannabine is only a makeshift. It is not to be employed except in extreme and rare cases, where our great alkaloids and their combinations (as morphine with hyoscyamine and strychnine, or hyoscyamine with

cicutine, strychnine and cocaine) are either not tolerated or remain without effect."

Dr. Elihu B. Silvers of New Jersey, used this remedy in connection with tolu as an anodyne, as a hypnotic, with compound tincture of benzoin in spasmodic coughs, with digitalis in dropsy, with potassium acetate in spasm of the bladder. It occurred to him that if it would readily induce sleep in nervous cases it ought to be useful in delirium tremens. He has now used the remedy for this purpose for forty years without the loss of a single case, although, as city physician, he has been called upon to treat many of the worst "drunks." He suggested its use to the director of the state asylum for the insane, in alcoholic mania, where it proved satisfactory.

Some years ago a doctor treated the morphine habit by making hashish eaters out of the victims. In the meantime we note in *The American Druggist* that out of five thousand two hundred and sixty-four cases of insanity treated in the Cairo Asylum, 27 percent were attributed to the excessive use of hashish. The doctor in question claimed that it had never been demonstrated that cannabis indica, used habitually, did any harm; and in this way excused himself for shirking his duty to his patients, leaving them in the grasp of a worse habit than that from which he pretended to cure them.

The full adult dose of a good extract is gr. 1-4. This may be repeated every hour till effect. With children the dose should follow the opiate rule, being relatively smaller than for adults. A granule of gr. 1-6 for adults and gr. 1-67 for children would meet the needs.

If the use of cannabis is followed by delirium it should be combined with veratrine, or with cicutine if movement is prominent. The hypnotic effect may be developed by adding a moderate dose of hyoscine, or of camphor monobromide. For its anodyne effects the addition of menthol for the stomach, hyoscyamine for neuralgia, acetanilid for headache, should prove effective. In fact, this is an admirable ingredient in the hands of the man who knows how to mix drugs to get their combined effects. Possibly the best combination would be with solanine or gelseminine.

CANTHARIDIN

Standard granule—Gr. 1-5000, Gm. .00012.

Cantharidin, $C_{10}H_{12}O_4$, constitutes from 0.3 to 0.5 percent of cantharides, from which it is extracted by chloroform. Cantharidin

is the anhydride of cantharidic acid, and crystallizes in rectangular, colorless plates, slightly soluble in water or in cold alcohol, readily soluble in hot alcohol, ether, chloroform or fatty oils. By taking up water cantharidic acid is formed, which unites with alkalis to form water-soluble salts. Cantharidin is by preference excreted by the kidneys.

Physiologic and Toxic Actions.—Liebreich attributes to cantharidin the essential effects of cantharides. He attributes the special effect of cantharidal vesication to the cantharidin absorbed. The salts in solid form are liable to decomposition, but potassium or sodium cantharidate can be administered by the stomach or hypodermically, in weak alkaline water solution.

Animals can be fed with hypotoxic doses for months without perceptible ill-effects. If the dose is increased but still kept below the toxic limit, the kidneys become soft, not hyperemic but serum-soaked, showing that the capillaries allow transudation of serum to an abnormal degree. Cantharidin has therefore a special action on the capillaries.

Are these merely passive channels for fluid-transmission, or have they a special function like other body-cells? Heidenhain showed that the capillaries can be specially influenced by chemical substances. At any rate, cantharidin coming in contact with the capillaries causes them to exude more serum. It may be inferred that the capillaries of each different organ functionate in their own special manner. As cantharidin in larger than the usual doses causes an excessive transudation, it may be assumed that in smaller doses it has a similar though imperceptible effect. If any organ is so diseased that the serum-secretion of its capillaries is impaired, cantharidin may tend to restore normal secretion, even in doses as yet too small to affect the kidneys injuriously. This increase of serum-secretion necessitates a large supply of nutriment to the affected cells, so that the latter are strengthened. Hence, cantharidin is useful when disease is due to external action, or to affections of the tissues. This explains the general tonic action previously observed as following the use of cantharidal blisters. This is especially the case when microorganisms attack the tissues, weakened by previous disease or traumatism. Pulmonary tuberculosis is especially a fit example. Petteruti reports three cures by cantharidin.

When toxic but not lethal doses are taken they cause gastric burning and pain, great thirst, the salivary glands swell and discharge freely, the pulse slows, diuresis and diaphoresis appear, with

strangury, tenesmus and diarrhea. The symptoms disappear in twenty-four hours, leaving no ill trace. In severer poisoning nausea and vomiting occur. The appetite may become ravenous, the pulse irregular, filiform and rapid. Urine is increased, with pain and strangury between micturitions, increasing as the urine becomes bloody, with leucocytes and fibrinous coagula moulded on the bladder wall. Consciousness is unaffected, but there may be trembling and perhaps convulsions. Even here recovery may follow rapidly.

In fatal poisoning there are acute gastritis and enteritis, spasm of the œsophagus, dysphagia; drinking is impossible as in rabies and atropine poisoning (Nothnagel); there is vomiting and violent diarrhea, bloody dysentery, the urine suppressed. Cantharides does not excite sexual activity, the severe priapism, turgidity and even gangrene of the penis it induces being in no sense pleasurable. In pregnant women it may cause abortion, without exciting sexual desire. Some authors fail to comprehend that irritation of the sexual organs is not the same as stimulation of the sexual sensation. A blister on the glans would not accomplish the latter object. These toxic symptoms are most frequently the result of cantharidal blisters. Large doses of cantharidin taken internally cause burning in the urethra and albuminuria. The latter often follows fly-blistering (Gubler), ceasing when the application is removed.

Small animals given cantharidin, Gram 0.01 (gr. 1-6), presented glomerulonephritis, the cells of the tubuli uriniferi congested, with hemorrhages in the renal and tubular tissues.

Nothnagel says pure cantharidin acts on the skin in doses of Gram 0.00002 in twenty minutes or less, the action occurring more promptly when oil is used as a solvent. If a spot on a rabbit's skin is painted with cantharidal collodion daily for two weeks the usual phenomena of blistering ensue, then the underlying vessels dilate, but the fat disappears; the deeper tissues, muscles, pleura and lung become anemic (Zuelzer).

Nothnagel attributes the affection of the genitourinary tract to the local action of the cantharidin excreted by the kidneys. Most cases of poisoning occur when it is given as an aphrodisiac.

Muerset states that the action of small doses is exerted entirely on the glomeruli, which are enormously dilated. Many leucocytes are found in Bowman's capsule. Albumin may be found in the urine half an hour after a hypodermic injection of cantharidin. Very small doses increase the excretion of urine, while larger doses lessen it. The interstitial tissue is little if at all affected.

Schachowa noted the presence of numerous bacteria in the urine when toxic doses were given, and these persisted until death. The reaction was alkaline. Fat appeared on the eighteenth day of the continuous administration of this drug. Albuminuria occurred only on the third day and not afterwards. He found the alteration limited to the epithelium of the tubuli uriniferi, which was discharged as epithelial and fatty casts. The glomeruli, capillary network, connective stroma and membrana propria were unaffected, save for slight thickening of the latter from maceration with serum. Small doses are excreted by the spiral renal tubules; larger doses by the part nearer the glomeruli and by the convoluted tubules, the part nearest the glomeruli functionating last. Only when the largest doses are given are changes observed in the rest of the uriniferous tubules, and these are least in the collecting tubes (Langhaus-Schachowa).

Radecki found large doses caused headache, formication, later on stupefaction, dyspnea, central respiratory paralysis, and death after general spasms, by carbonic acid poisoning.

Dragendorff recovered cantharidin from the putrid body of a cat eight days after death. Muscular tissue from chickens fed on cantharidin killed a cat with the characteristic symptoms.

Brunton states that cantharides affects the trachea and larger bronchi, causing congestion and irritation. It appears, therefore, that cantharidin is eliminated by all the mucous membranes, as vesication in the alimentary tract has been found even when the drug is administered hypodermically (Cushny).

Therapeutics.—In doses of one minim of the tincture, cantharides checks hematuria; in large doses it increases the disease (Brunton). It should be given if at all, only in passive renal hematurias.

In acute nephritis, when the acute symptoms pass and a little albumin and blood are still to be found in the urine, it is very useful in doses of one to three minims, every three hours (Brunton).

In lupus, cantharidin was injected hypodermically by Liebreich, curing incipient and lighter cases completely. In other cases where nutritive disturbances were marked, this agent acted beneficially. Its use must be methodical. It is contraindicated in renal disturbances, but if the kidneys are sound the drug may be given for years without disturbing them or causing any other observable ill-effect. The dose accurately fixed in any given case, may be administered for years without alteration, though the least increase is ill borne, producing dysuria and diarrhea.

It is useful in cystitis when there is inability to retain the urine, and in ordinary incontinence of urine, though atropine is generally better (Brunton).

Chordee is often relieved by a drop of the tincture three times a day (Brunton).

Cantharides, one part of the tincture to eight, is a useful lotion for promoting the growth of the hair (Murrell).

Large doses are useful in impotence of elderly men (20 minims thrice daily, after meals), but accessory treatment is desirable (Murrell). This is a very dangerous dose.

Small doses cure the slight incontinence of urine in women, leakage from the bladder occurring with cough (Murrell).

In doses not exceeding 0.12 to 0.18 c. c. (m. 2 to 3) the tincture has been commended in pyelitis, cystitis, gleet and leucorrhea. It is contraindicated in acute inflammation; it has succeeded in atonic amenorrhea, and has suppressed passive atonic seminal emissions. There is some evidence to show that the internal administration may check the progress of cancer (Shoemaker).

Full doses are useful in impotence from old age, sexual excess or masturbation (Ringer).

In simple and tubercular laryngitis potassium cantharidate causes serous exudation, which is speedily reabsorbed. Hoarseness diminishes and swallowing is easier (Liebreich).

Hennig applied cocaine cantharidate locally in tuberculosis, ozena, and mucous syphilis; three to six parts in 2,000 of chloroform water.

Cantharis has been given internally as a systemic stimulant after debilitating fevers (Shoemaker).

In late stages of nephritis, with relaxed, torpid kidneys, or where albuminuria comes after slight exertion, tincture of cantharides Gram 0.05 (m. 1) thrice a day, is of great service; also in chronic alcoholic nephritis, irritability of the bladder in women and children with depression, very chronic gleet and prostatorrhea; internally in psoriasis, eczema, lichen and prurigo (Hare).

Its administration in cholera and epilepsy has fallen into complete disuse.

Diabetes insipidus has been arrested by the internal use of cantharides; it is also useful for menorrhagia in weak women (Butler).

It is of some benefit in dropsies, especially following scarlatina; in the later stages of diabetes, and in acne with uterine irritation (Ellingwood).

A careful study of the literature of cantharides shows that the active principle is largely excreted by the kidneys, to a less extent by the gastrointestinal mucosa and slightly if at all by the respiratory tract. I have been unable to find any conclusive or even probable evidence to show any action whatever apart from the local effects produced on the mucous surfaces and other tissues by which the drug is excreted. The therapeutic effects are therefore to be exclusively attributed to this local action. Even the succulence of the tissues described by Liebreich comes under this head, and he describes none of this beyond the excretory membrane. In states of relaxation and debility of the genitourinary organs we may expect from cantharidin the same stimulant effect exerted on a cutaneous ulcer by a weak solution of silver. This applies also to the uterus, and the endometrium probably excretes and is stimulated by cantharidin. To a less extent the lower bowel is similarly affected by this agent, and in relaxation of the rectal tissues, prolapse and passive hemorrhoids, chronic catarrh and ulcer of the rectum, cantharidin should be a useful stimulant if the dose required do not prove too irritant to the urinary mucosa. Consequently I very strongly doubt if doses large enough to favorably affect the respiratory mucosa can be given without harm to the kidneys, since very little of the drug is excreted by the lungs. Beyond these organs I am unable to find any reason for the administration of cantharidin.

In regard to its effect as an aphrodisiac the evidence is conflicting. Most authors deny that there is any excitation of the sexual appetite, the priapism being only caused by toxic doses, and as a symptom of serious poisoning. I have given the drug many times in moderate doses without eliciting the slightest pleasant sexual sensation; and in the only cases where erections were produced the suffering was too great to admit of any thought of pleasure. When impotence is attended with relaxation of the genitourinary tissues, moderate doses of cantharidin may be useful in imparting tonicity, and the drug may be of some value as an adjuvant to strychnine, but nothing more; and of the two strychnine is preferable, since there will be also then present atony of the whole body, including tissues not influenced by cantharidin. And it would not be politic in such cases to restore the strength of this function while the more vital processes are left in a state of debility.

Cantharidin must be looked upon as a highly specialized weapon, delicate and keen-edged, capable of doing much good in a limited group of affections, but dangerous in unskilled hands. It is strictly a drug for dosimetric administration, and should never

be given in rare large doses, but in minimal quantities rapidly repeated, until the beginning of burning in stomach or urethra shows the physiologic limit to be reached. And as many of the beneficial effects of fly-blisters are due to the cantharidin absorbed, its internal administration may well replace the blister in many instances.

We here meet the same cogent query as in the case of arsenic. Having determined that cantharidin exerts its power upon certain selective cells, in the physiologic state, as above shown, is this power exerted curatively upon these cells when diseased? Were our knowledge complete of the intimate nature of disease-processes, as affecting each tissue, each variety or group of cells, this question might be answered *a priori*. As it is, the only way to determine the truth is by actual trial. There is here room for very extended experimentation, to confirm or disprove the clinical observations of earlier days, when medicinal agents of uncertain and shifting strength and composition were employed, and the difference between *post hoc* and *propter hoc* was little regarded.

Especially I would recall attention to the claim recorded by Shoemaker, of the arrest of the growth of cancer by cantharidin. This is too important to be permitted to go without investigation. As in lupus, when the cancer is within reach it would be best, perhaps, to inject the solution hypodermically into the neoplastic growth. For this the combination known as cocaine cantharidate is suggested. This is said to be a mechanical mixture like caffeine citrated, not a chemical union; but the resultant mass is freely soluble in water, which cantharidin is not.

As to the value of potassium cantharidate in tuberculosis, Nothnagel condemns it; but condemnation is habitual with this writer, who rarely finds good in any remedy. Petteruti's three cases were abandoned by him as failures, but on examining them some time later he was surprised to find them cured. A true pessimist would not have made the final examination but suffered the cases to go on record as failures.

Liebreich gives the dose of cantharidin as Gram 0.0002 to 0.0008 (gr. 2-667 to 1-85), well diluted. Sodium cantharidate is injected into patches of lupus. Dose 0.0001 for adults, every other day, suspended if diarrhea or dysuria occurs.

Dietrich's cantharidin oil is composed of one part cantharidin, 960 parts of olive oil and 40 of acetone.

Schroff fixed the lethal dose of cantharides for man at Gram 2.0 (gr. 30), but of course the toxicity of various specimens varies greatly.

For use by the dosimetric method the adult dose may be placed at Gram. 0.00001 (gr. 1-6000) repeated every hour until slight burning is felt in the stomach or urethra.

CAPSICIN

Standard granule—gr. 1-134, Gm. .0005.

Some day we will realize the importance of that great aggregation of nerve ganglia to which Byron Robinson gave the name of the Abdominal Brain; and when we do so the value of capsicum will be also appreciated. The Eclectics have done so, and the rich therapeutics ascribed to this remedy by them contrasts notably with the poverty of the same as found in our own works.

Capsicum contains a crystalline principle on which its activity depends, but probably the most efficient concentration to be found in the markets is the oleoresin, which is active enough for all practical purposes.

In all tropical countries capsicum is used as a condiment, or rather as a dietary article of daily consumption, in quantities that would appear fabulous to the resident of colder lands. That there is a reason behind this no one will deny; but whether it is because the climate renders advisable an equalization of the inner and outer heat, or the digestion fails without such powerful stimulus, or that it acts as a check on the growth of gastric flora and fauna, is a matter of conjecture. Certain it is that the Caucasian removing to the tropics soon falls into the ways of the country and takes his *chile con carne*, hot tamales, curry, and other hot concoctions like the native.

But whether this practice does or does not conduce to longevity in the native or habitant of the tropics, it is certain that in the temperate zone it is calculated to wear out the digestive functions and shorten the working life of the stomach and liver. The writer recollects a well-known citizen of an eastern city, who was accustomed to call at the restaurant for a raw steak, which he would punch full of holes with an instrument he carried for that purpose, fill the holes with capsicum till the quantity almost equaled that of the meat, and thus eat it. He is dead!

If the digestion requires the stimulus of capsicum, it requires still more the attention of a physician who understands the digestive system, if such an one may be found, and a really scientific regulation of diet, exercise, and the personal hygiene in general. But it seems preferable to the multi-millionaire to resort to tabasco. Well, if

this shortens his life, we see in it another exemplification of that law of compensation of which life shows so many cases.

Fifteen years ago three men were rivals in their spheres, as professors of the same branch in three medical colleges in one city. One recognized when he had enough, and drew out, leaving the field to his victorious rivals. They are dead; have been for years, while he still lives and enjoys health and we trust usefulness.

Which was victorious?

The most important function of capsicum, and the least appreciated, is as a stimulant to the solar plexus, rousing the vitality and awaking the vital resistance to the onslaught of disease. In the collapse of choleras, the chill of malarias or other sudden and powerful infections, in the algid stage of tropic dysentery, the influence of a decided dose of capsicum thrown into the stomach is something to be appreciated when once seen.

What is the physiologic effect? In small doses it is followed by a sense of warmth in the stomach, the secretion of gastric juice is stimulated, and all the digestive functions are aroused. Of course the frequent repetition of this in time wears out the susceptibility of these organs, they cease to secrete without the capsicum, and gradually it loses its effect, so that the digestion is worn out.

In very large or toxic doses capsicum causes vomiting, giddiness, purging, pain in the stomach and bowels, acute gastritis and intoxication, with feebleness of the nervous powers.

The dose necessary to produce such effects depends largely on the patient's habits. If his stomach has been seared by long indulgence in stimulants or condiments, it requires very large doses; if unaccustomed to them, we should be cautious in administering the doses hereinafter recommended.

Therapeutics.—The list of affections for which capsicum has been recommended is long.

Colds: Capsicum in hot infusion is one of the domestic remedies to break up a cold. It ranks with the hot toddies, etc., and is open to the same objections that they increase vascular pressure and thus add to the hyperemia of the affected tissues. The use of the depleting method, abstracting fluid by glycerin from the swollen tissues directly, or from the blood by eliminants, will soon prove itself the better way. But when one has been exposed to cold while riding, and comes into the house chilled, a bowl of red pepper tea will arouse the vital resistance and send the blood equally through the vessels and prevent a threatened congestion, as well as any other stimulant, and better than an alcoholic beverage.

In catarrhs of the pharynx the use of capsicum as a gargle is of value in arousing the diseased and weakened tissues to a healthier grade of action. The same remedy has proved effective in relieving hoarseness.

In atonic dyspepsia and chronic gastric catarrh, capsicum in small doses is a valuable stimulant, and aids the digestion while other measures are restoring the strength.

In delirium tremens capsicum, in doses of twenty grains to sixty, will do more to secure sleep and restore the nervous system to its balance than any of the direct hypnotics, singly or combined. In fact, the use of capsicum was the writer's main reliance until the true treatment of this malady by elimination was comprehended. When a man is crazy for drink, insisting on repeated drams till drunk, hardly waiting till one is down till he is calling for another, give a teaspoonful of capsicum in an ounce of whisky. It will divert the mind into a different channel—mainly that of swallowing ice—and instantly stops the calls for alcohol. From this huge dose we have never known harm, but of course it has only been called for in inebriates, whose stomachs were well prepared. But the administration of 1-10 grain of c. p. emetine is better, if the patient can be kept quiet till it puts him to sleep.

In the algid forms of malaria, congestive chills, a full dose of capsicum will do more than any other remedy to arouse reaction. It will require but half the dose of quinine, or less, to do the work when capsicum is added.

The atonic dyspepsia of drunkards is usefully treated by capsicum, taken freely as a condiment. Here the effect is partly due to the stimulation of digestive secretion, partly to relief of the tormenting thirst, and partly to a direct action of the drug in stimulating the nervous system. There is also an effect on the liver that is of value.

In chronic congestion of the kidneys capsicum is said to diminish the irritation and increase capillary activity; but here the writer has had no experience. When the kidneys require stimulation of the dialyzing membrane it unfortunately happens that they will not bear it. Very small doses of any volatile oil, like juniper, will increase the excretion, but if the dose is increased the excretion is apt to fail at once in a disquieting manner.

In passive diarrheas, and when a general stimulant is indicated, capsicum carefully given is very beneficial.

Torpid, sluggish forms of piles are helped by capsicum, which arouses a healthier circulation.

In all the formulas for chronic or habitual constipation capsicum forms a useful ingredient, aiding to arouse a healthier state of feeling in the intestinal mucosa, and rendering other remedies more effectual.

In dysenteries with vesical tenesmus, laxity and weak digestion, capsicum has been found beneficial. It is of course not suited for the acute stages, where the indication is to sedate abnormal irritability; but when the tissues threaten to fall into sphacelus from the intensity of the infection, or when the malady continues from deficient vitality, capsicum is the most potent remedy.

The same may be said as to its use in low fevers. If the vitality were sufficient the tissues would throw off the disease and take on reparative action; and then capsicum may succeed in arousing the remaining forces. It is obvious that the condition should be thoroughly comprehended before such a remedy is administered. The man who assumes that capsicum is "good for dysentery" had better let it alone.

In organic paralyses with digestive torpor the use of capsicum improves the digestion, and this reacts on the paretic affection in a way that has given the treatment repute, with those who do not appreciate the value of a good food supply, well digested, and the prevention of autotoxemia, in such cases. Capsicum is best for temporary use, not habitual.

The value of solar plexus stimulation is nowhere shown to better advantage than in the group of choleras, Asiatic, morbus and infantile. When the stage of collapse has supervened, nothing equals capsicum in arousing the vitality and restoring warmth to the skin. Full doses must be given, the tincture, undiluted, being advisable. For here the admonition of the Hindoo doctors is wise—if you can give a dose strong enough to bring the tears to the eyes the patient will be saved. And this principle comes in as applicable to the first onslaught of the malady, as well as in dysenteries and the chills of opening fever attacks.

The same principle is applicable to angina pectoris, whose paroxysms may be broken by a single dose of capsicum if strong enough. The timid practician is out of place here—it is the sledge-hammer blow alone that will save life.

In the debility of advancing age, with tired, aching muscles, stiff joints and general relaxation, capsicum is of much value. Here is the place for it as a condiment, for those who have wisely refrained from its use in earlier days. Give enough for the work.

In pneumonias, debilitated cases, where there is a threatening of the affected pulmonary tissues falling into abscess, capsicum in large doses may arrest the destructive process.

In flatulence, capsicum should be added to the aloin, strychnine, eserine or berberine prescribed, and from these an effective formula may be made up.

In some cases of persistent vomiting it seems as if the stomach requires a lesson—for in what other way can we explain the credit the following "antiemetic drops" possess? One-half oz. powdered capsicum, two drams of salt, 1-2 pint each of vinegar and water; dose a tablespoonful.

In various spasmodic maladies capsicum has proved effective; here full doses with as little dilution as possible are best.

For passive hemorrhages, especially uterine, capsicum has been advocated; and associated with ipecacuanha in postpartum cases.

Locally, capsicum has been recommended as a gargle in scarlet fever and in chronic tonsillitis; as an application to stimulate sluggish ulcers; for chronic ophthalmia, where the use is as apt as that of abrus (jequirity), and indubitably less dangerous; for corneal ulcers, where the vitality of the tissues must be sustained at any cost; to abort acute tonsillitis, used very early in the attack; for the hoarseness of atony of the vocal apparatus; for relaxed uvula; chilblains; toothache; cold feet; in any case where it is advisable to stimulate the vitality, or to increase the action of other drugs—the latter applying to local or internal use equally.

The specific indications for the use of capsicum are thus summed by King: Great depression and debility; atonic dyspepsia of drunkards; delirium tremens; colic with flatulence; congestive chills; cold feet; white lips, small pulse, capillary atony, tongue dry; chronic hemorrhoids.

For most of its uses the oleoresin of capsicum is eligible; in doses of gr. 1-20 to a grain, before meals or as indicated. When it is desired to powerfully affect the stomach and solar plexus, as in congestive chills, a grain or more may be given in a teaspoonful of alcohol. For cold feet powdered capsicum may be put in the stockings. The red pepper of the grocer is rarely if ever undiluted, and that of the pharmacist is not much better. If the physician will take the trouble to secure a supply of a pure article he will be surprised to find what a difference exists. Since the Pure Food and Drugs Act has come in, we have much better spices and peppers, but there is still much low-grade capsicum in pharmacies and groceries.

CASCARIN

Cascara is a substance of complex chemistry, containing resin, emodin, isoemodin, two percent of tannin, glucose, a fixed oil, a volatile oil, rhamnol, a non-laxative hydrolytic enzyme, and a substance yielding syringic acid on treatment with acids (*Amer. Disp.*).

While the evacuating effect of the bark of rhamnus purshiana is well known, its active principle was unknown till discovered by a process lately described in an English patent. The commercial preparation of Beprince consists only of the dried extract of the bark.

The following process gives the hitherto unknown glucoside: An aqueous or alcoholic extract of cascara sagrada is treated with lead acetate as long as a precipitate continues to be formed. This precipitate, which amounts to about 70 percent, and is inactive and valueless, is placed on a filter and washed repeatedly with water. The total filtrate is mixed with basic lead acetate and ammonia by which means nearly all the active substance is precipitated out. The latter well-washed precipitate is then suspended in water and treated with sulphureted hydrogen, and the watery solution of the active substance obtained after filtration is evaporated to dryness *in vacuo*. The residue thus obtained, a light yellow pulverulent substance, contains only traces of ash, tastes slightly bitter, dissolves easily in water and in glacial acetic acid with a yellow color, and dissolves with difficulty in alcohol out of which latter it separates in microcrystalline powder. The aqueous solution reacts acid and reduces Fehling's solution when warmed, but with phenylhydrazin it yields no crystalline combination. Concentrated sulphuric acid dissolves it with a brown color. The effectiveness, which is twenty times stronger than the cascara bark, was positively confirmed by physiologic and clinical tests (*Chem. Zeitung Repert.*, 1908).

Cascara increases the secretions of the whole gastrointestinal canal, improves appetite and aids digestion. As a laxative it also increases peristalsis, and its use in proper doses is not followed by reactive constipation. As habitual regularity in alvine evacuation is established the dose may be gradually decreased.

In one case, a bedridden woman who had ballooning of the rectum, cascara was given for five years in similar dosage without failing in action, but the dose could not be reduced. There is little or no tendency to griping from pure cascarin, but some other elements of the bark are irritant. The long-continued use of this

drug tends to induce hemorrhoids, and a few doses may arouse quiescent piles to pernicious activity. Too large doses induce griping and irritation, the effects closely resembling those of aloes.

Lloyd says cascara has done well in sick headache, which is natural since this is usually toxemic. In small doses it acts as a rectal tonic, relieving the relaxed form of chronic hemorrhoids, as does aloin; but with either it is easy to overdo and excite distressing acute exacerbations. This remedy was urged as an antirheumatic, and its success was a factor in directing attention to the importance of the intestinal conditions in this malady. Cascara has no virtues here beyond other laxatives. It has proved of value when judiciously given in chronic diarrhea with sluggishness of the liver, and gastric duodenal and hepatic catarrh with jaundice—the whole group probably dependent on the retention and decomposition of feces, with toxin absorption, overworking the elimination.

Felter and Lloyd give as the specific indications: Constipation due to neglect or nervous and muscular atony of the intestinal tract; lesser ailments depending solely upon constipation, with intestinal atony.

Like other remedies for habitual constipation cascara is best administered in small, divided doses. The exact quantity necessary to secure a full movement should be divided into three doses, each to be taken an hour before meals, with a glass of water. Cascara is too slow in action for use as a cathartic. It is sometimes advisable to give it with similarly acting remedies. A combination of cascara with bilein, aloin, podophyllin and leptandrin, adding minute quantities of strychnine, atropine and capsicin, would be widely applicable.

The average adult dose of cascarin alone is one grain daily, or 1-3 grain three times a day. A sense of soreness in the bowels follows doses too large for the patient.

Quite recently a glucoside prepared from the bark of cascara sagrada has been put on the market under the name of peristaltin, for hypodermic use. It has been favorably commented upon, for instance by Walther.

CAULOPHYLLIN

Standard granule—gr. 1-6, Gm. .01.

Caulophyllin is a concentration from the rhizome and roots of Caulophyllum thalictroides, the blue cohosh, squaw root, or papoose root.

The virtues of this plant depend on a crystalline glucoside isolated by Lloyd, and by him named leontin. It is slightly soluble in cold and very soluble in hot alcohol, insoluble in water or in chloroform. Alkaline watery solutions dissolve it perfectly. The solutions are acrid and irritating. Of the caulophyllin of the market Lloyd says: "Like nearly all the socalled concentrations and resinoids of early Eclectic preparation, while they were better agents than preceding pharmacal products, yet at the present time they are too uncertain in composition and medicinal value to hold a leading place among our more modern therapeutic preparations." And that tells the story of the alkaloids, which, however, this great chemist is not yet ready to accept.

Therapeutics.—Caulophyllum was introduced by Rafinesque as a powerful emmenagog; the Indians used it in rheumatism, dropsy, colic, sore throat, cramp, hiccough, epilepsy, hysteria, metritis, etc. King applied it for aphthous stomatitis. Scudder believed it influenced the hypogastric plexus, affecting the circulation, nutrition and functions of the reproductive apparatus. Lloyd describes it as antispasmodic, diaphoretic and diuretic, expectorant, emmenagog and parturifacient. The Indians gave it some weeks previous to confinement to facilitate labor. During labor it relieves false pains and coordinates true ones, increasing their force. It is a better oxytocic than ergot, stimulating normal contractions instead of inducing spasmodic action. It is best when delay is due to debility, fatigue or lack of nervous energy, and when with weak pains the tissues feel full and congested. He advises it for several weeks before labor, for delicate women or those who have prolonged and difficult labors. Hale says those who take caulophyllin thus may overrun their time by 12 days, but have very easy labors and make good recoveries.

Felter and Lloyd enumerate the following conditions in which caulophyllin gives benefit: After-pains, especially spasmodic; hour-glass contraction, spurious labor-pains; it is antiabortive by relieving the irritation on which the trouble depends; for irritation of the reproductive organs resembling congestion, chronic inflammations and debility; uterine tenderness and pain with debility; to overcome attacks of hysteria, relieve ovarian or mammary pain or irritation in hysteria; chronic endometritis or metritis, ovaritis, ovarian neuralgia, uterine leucorrhea, amenorrhea and dysmenorrhea; uterine rheumatism with nervous excitement, menstrual cramps and menorrhagia due to subinvolution; chorea and epilepsy with maladies of the sexual organs, flatulent and spasmodic

colic, cramps; obstinate hiccough; its antispasmodic effects are permanent; it lessens irritation in cystitis, urethritis, chronic nephritis, spasmodic retention of urine, in rheumatics; when crampy pains in stomach follow eating; rheumatism of small joints, asthenic plethora and its rheumatic pains; insomnia, bronchitis and catarrhal pneumonia as a sedative; orchialgia; gastric nausea and vomiting. Leontin has been used with benefit in the amenorrhea and dysmenorrhea of chlorosis.

Specific Indications.—Uterine pains, fullness and weight; pain in legs; fullness of tissues as if congested; irritable debility of the nervous system with muscular weakness; spasmodic muscular pains, articular pains, rheumatic pains of asthenic plethora, epigastric and umbilical colicky pains; dull frontal headache; great thirst; as an oxytocic; false pains and uterine irritability; sexual erethism; spasmodic uterine contractions; dysmenorrhea; irregular menstruation; stomach cramps after eating; pain in toes and fingers not due to tissue changes.

Ellingwood says this remedy must be continued long to obtain its benefits. The last three months of pregnancy constitute its great field. Gestation being prolonged the fetus is fully developed and labor normal. He gives caulophyllum with confidence for the amenorrhea at the beginning of menstrual life; to control congestion in whooping-cough; for moth patches on the face; rigid os; atonic hemorrhagic tendency after labor; dysmenorrhea or lack of development; dropsy with menstrual disorders. A dose is given every ten minutes till labor pains become sufficient.

Dr. E. J. Meacham verifies these statements as to the value of caulophyllin in labor, and tells of a case in which there was active labor with the soft parts hard and resisting dilation. It was a primipara. He gave caulophyllin gr. 1-6 every fifteen to thirty minutes and soon found the os soften and dilate.

The eclectic school is practically unanimous as to the value of this drug, and as to the conditions in which it is indicated. It seems unlikely, to say the least, that all this testimony is mistaken, and that caulophyllin is unworthy a place in modern medicine. Cushny attributes any virtues it may possess to its saponine and Shoemaker refers to this agent some expectorant properties which he attributes to blue cohosh. The limited uses made of caulophyllin by the writer have been sufficient, however, to convince him that it is an active agent and so far as this experience goes, to confirm Ellingwood's recommendation. The concentration caulophyllin fully represents the plant's therapeutic powers, though

leontin should be still better if it could be procured. It is not offered in the drug market.

In acute conditions caulophyllin should be given in doses of gr. 1-6 dissolved in hot water, every ten minutes, till effect. In chronic conditions give a grain four times a day, in granules to allow slow absorption.

CEPHAELINE

In 1894 Paul and Cownley succeeded in separating emetin (total alkaloid from ipecac) into two components—cephaeline, and an alkaloid for which they retained the name "emetine." The formula $C_{15}H_{22}NO_2$ has been assigned to the cephaeline, and $C_{14}H_{20}NO_3$ to the emetine of these investigators.

R. B. Wild (*Pharm. Jour.*, 1895, p. 435) has made careful pharmacologic experiments with cephaeline. He finds that 5 milligrams (1-12 grain) produce nausea, slight dizziness, salivation, and retching but not actual vomiting; at the same time the arterial pressure is somewhat diminished. A dose of 10 milligrams (1-6 grain) produces similar effects, followed in an hour by violent vomiting; occasionally intestinal peristalsis is increased, a soft stool resulting. No appreciable influence on the nasal mucosa, skin or urinary system has been observed, and the vomited matter does not contain an excess of bile. Furthermore, cephaeline is reported to have but a moderately toxic action on the voluntary muscles; the walls of the blood-vessels are not excessively contracted, and the nervous supply of the heart is also not affected in an unusual degree.

CERIUM OXALATE

Standard granule—gr. 1-6, Gm. .01.

The cerium oxalate of the markets contains also didymium, lanthanum and other earths. Some specimens contain very little cerium. Some years ago a chemically pure article was offered but nobody could be found who was willing to pay the necessary price, purity at that time not being properly appreciated. Much of the disrepute into which this remedy has fallen is due to its uncertain composition as offered by the pharmacies.

Cerium oxalate was introduced by Sir James Y. Simpson, as a remedy for the vomiting of pregnancy. It is white, odorless and tasteless; insoluble in water or in alcohol. Large doses cause dryness of the mouth. Cushny says it depresses the heart, causes vomiting and purging, with hyperemia and ecchymoses of the

stomach and bowels, nephritis and congestion of the kidneys, when administered intravenously. Shoemaker pronounces it a sedative to the gastric mucosa.

This salt has held a precarious place as a remedy for the vomiting of pregnancy, opinions varying as to its efficacy. Those who look on this ailment as a disease to be treated *per se*, will not succeed with it. But when the bowels have been regulated, the function of the kidneys brought up to the full measure of efficacy, and rhagades and other affections of the uterus properly treated, the oxalate of cerium will prove the best of the direct gastric sedatives.

But if inflammatory or other irritations of the stomach are the cause of the vomiting it is doubtful if this remedy will give relief. Hare speaks of it as a remedy for acidity. Shoemaker says it has been given for vomiting of uterine disease, and even for that of gastric cancer; as well as for the obstinate vomiting of typhoid fever and that of phthisis. The nausea attending the administration of opiates has been relieved by cerium. Image, who recommended it highly in uterine vomiting, says failure is due to the use of too small doses. He gave gr. x, repeated every hour.

Clarke and Morje found cerium serviceable in whooping-cough, lessening the severity and the frequency of the paroxysms. Shoemaker speaks of its value in the severe cough of phthisis, or of chronic bronchitis. It has also been used with benefit for the dyspnea due to deficient innervation of the stomach, and in chronic diarrhea. Less certain is its use in chorea, epilepsy and dysmenorrhea. Simpson gave the nitrate for irritative dyspepsia with gastrodynia and pyrosis.

The fact seems to be that the oxalate of cerium is a direct sedative to the stomach mucosa, not suited to cases of acute inflammation or irritation. This irritability may be due to autotoxemia, to deficient renal elimination, or to cerebral irritability. In which of these is cerium indicated? It has seemed to exert a direct sedative effect on the gastric terminals of the vagus. More accurate observations should be had to determine why this remedy which acts so brilliantly in some cases fails in others apparently similar.

Image recommended that the first dose—of gr. v—should be taken before rising, and found three doses a day usually sufficient. This is best for vomiting of pregnancy, and for gastralgia. In acidity and other forms of recurrent vomiting, a smaller dose, gr. 1-6 to j, repeated every five to fifteen minutes, gives better results. Wood, who is a megalodoser, gives five grains every hour.

CETRARIN

From Iceland moss is derived cetrarin, or cetraric acid, $C_{18}H_{16}O_8$, an intensely bitter principle forming hairlike needles. The moss is treated with petrol-ether, precipitated with potassium carbonate and purified with hydrochloric acid. Cetrarin is insoluble in water, slightly soluble in ether or cold alcohol, readily in boiling alcohol, in alkalis and their carbonates.

Merck terms cetrarin a hematinic, stomachic and expectorant, useful in chlorosis, where it increases the number of red-blood cells; also in incipient phthisis, bronchitis, and digestive disturbances with anemia. Dose, Gram 0.1 to 2.0, gr. 1 1-2 to 30.

Kobert states that cetraric acid increases intestinal peristalsis, and augments the number of both red and white blood-cells, especially when they have been diminished by disease. It slightly stimulates the central nervous system, and increases the secretion of saliva, bile and pancreatic fluid.

In Iceland the moss is employed as a prophylactic against elephantiasis. Eckfeldt recommended cetraric acid as a remedy for hemoptysis, and it has also been applied locally for epistaxis and for spongy gums.

As Merck lists cetrarin at 75 cents a gram, it is obviously beyond the reach of ordinary patients. Nor does it seem to be necessary to employ this principle, as probably all the benefit it affords will accrue from the use of Iceland moss as a food. This can be prepared as a jelly, flavored to suit the taste, with sugar, salt, or lemon; or used as a beverage. But it is important to know that this rarely used food contains such valuable remedial properties.

In pernicious and intractable forms of anemia the cost may be disregarded, and this substance may prove most valuable at a period when other remedies fail.

CHELIDONIN

Chelidonium majus, the greater celandine, is one of those plants that is continually being brought forward as a remedy, insufficiently tested, and allowed to drop back into obscurity. In this case it is as a remedy for cancer that the plant is advocated.

Closely related to the poppy, chelidonium rivals that storehouse of remedial agents in the number of active principles it contains. Schmidt announced that in celandine he found no less than 12 bases. Among these were chelerythrine, chelidonine, chelidoxanthine, and protopine. Concerning the properties of

these principles our information is scanty and uncertain. Chelerythrine is said to be identical with sanguinarine, which it closely resembles in physical properties. But this identity has been denied. Such assertions should always be taken with distrust. Identity of ultimate or of elementary composition is not necessarily identity of remedial action. Even in the case of theine, which Merck asserts to be identical with caffeine, so good an observer as Mays finds a decided difference in their therapeutic effects. Scopolamine is asserted to be identical with hyoscine, and this also is denied.

Merck gives the following data as to chelerythrine: Soluble in alcohol, ether, chloroform, benzine and petroleum oils; a cardiac poison. Sanguinarine is soluble in chloroform, amylic alcohol, benzine, alcohol and ether; stimulant, tonic, expectorant, purgative, emetic; dose gr. 1-12 to 1-4. Poison! The nitrate is soluble in water and in alcohol. Chelidonine is an alkaloid, white, crystalline, soluble in alcohol, chloroform, very slightly in ether, insoluble in water; non-toxic; narcotic, resembling morphine but less stimulating, slightly stimulating the spinal cord.

Sollmann says that the group containing chelidonin cause paralysis of the sensory nerve ends like cocaine. They also paralyze the ends of striated muscle, so that faradization induces alternate contractions and relaxations instead of tetanic continuous contraction. The heart muscle is depressed, the pulse weak and slow, the respiration stimulated.

Therapeutics.—Ribbing and Ruempf used chelidonin in gastric ulcer, cancer and enteralgia, in doses of 2 to 5 centigrams. The results were quite satisfactory, in some cases even excellent. One advantage over opiates is that chelidonin produced no trace of heaviness, somnolence, constipation or other concomitant phenomena. Especially in infantile practice chelidonin was accorded preference over opium for its innocuity. With adults the dose of chelidonin is Gram 0.10 to 2.0 or more.

It possesses calmative and hypnotic properties, while being less narcotic than the other alkaloids obtained from plants of the same family, such as the opium derivatives. It is precisely this small degree of toxicity that indicates the use of chelidonin in certain painful affections of the stomach and bowels.

Ellingwood pronounces chelidonium a drastic cathartic, violent local irritant, alterative, diuretic, diaphoretic, expectorant and vulnerary. It is applicable in fully developed abdominal plethora, inefficiency of the abdominal glands, sluggish circulation in the abdominal tissues, glands and organs. It acts well with leptandrin,

podophyllin, iridin, chionanthin and sodium phosphate; when there is lessened secretion of bile, as shown by acholic stools that float, with or without jaundice, and its concomitant symptoms. Sluggishness of the portal circulation induces slowness of the pulse, palpitations, weight, stiffness and swelling of the extremities, pale doughy skin, local and general edema, dull pain or constant aching of limbs and muscles, aching in forehead and occiput, vertigo, weariness, irritability, inactivity, constipation and diarrhea, erratic colicky pains, sallowness, jaundice, etc.; and for these chelidonin is an excellent remedy. Many physicians, after thirty years' use, consider this the best remedy for gallstones. Much evidence has accumulated of its efficacy as a local application to warts and epitheliomas; also in urticaria, eczema and itching eruptions.

Felter and Lloyd say chelidonium as a drastic fully equals gamboge. It is applied as an irritant to indolent ulcers and fungous growths, to remove opacities from the cornea, and to cure ringworm. It is superior to arnica as a vulnerary, to subdue traumatic inflammations, and for scrofula and hemorrhoids. It is supposed to influence the spleen especially. It acts on the parts supplied by the solar plexus. These authors enumerate as favorably influenced by this remedy acute and subacute hepatitis, without suppuration; migraine, bilious headache, supraorbital neuralgia, bilious dyspepsia with headache, all gastric and intestinal disturbances due to faulty action of the liver; "liver coughs," hemorrhoids, hepatic and splenic congestion, capillary engorgements of the abdominal viscera; biliary catarrhs, obstructive jaundice, full tensive throbbing pain in the right hypochondrium, pain extending beneath the right scapula. Scudder used this plant when the tongue was pallid and enlarged, skin sallow, full, greenish-yellow, mucosa relaxed and full, right hypochondrium full, abdomen tumid, feces light colored, urine pale but heavy and cloudy. An added indication is edema of the feet.

Specific Indications.—Full, pale, sallow tongue, and mucosa; skin pale, sallow, sometimes greenish; hepatic congestion; jaundice due to swollen bile ducts; sluggish hepatic action, cough with hepatic pain, fullness with tensive or throbbing pain in the right hypochondrium, extending to right shoulder; melancholia, headaches, gastric disorders dependent on deficient liver action.

We have here the action of an effective cholagog cathartic. Chelidonin is something more; but we must wait till the rapidly awaking interest in drugs reaches the point when the vegetable

world will be called upon to unlock its treasuries and put its long-hidden riches into circulation.

Robinson made injections of chelidonin in a woman presenting a malignant tumor of the superior maxilla with large intrabuccal ulceration. Three hours after the injection reaction followed, intense, with shivering, but next day the tumor began to soften. The dose was increased and the tumor bathed twice daily with ext. chelidonium and an equal part of glycerin. The tumor has continued to decrease and is no longer inflamed. He deduces a specific action of chelidonin on malignant tumors.

Ivanow cites the case of a woman aged 53, with gastric cancer, treated by chelidonin internally. Her condition was one of profound marasmus with violent pains in the stomach, vomiting all food so persistently that rectal feeding was necessitated. The vomitus had the appearance of coffee grounds; the liver was enlarged, the left lobe prominent. The existence of a malignant neoplasm was beyond doubt. Under the influence of chelidonin she improved rapidly, the vomiting that had persisted for three months ceased in fifteen days, the tenderness of the tumefaction as well as the gastric dilatation subsided and the appetite returned. Soon she could feed herself by the mouth and get up; she suffered no longer and returned to her occupation.

A lively reaction followed the administration of this medicament. The observed phenomena, local and general, have a characteristic clinical significance. The reaction had a certain general resemblance to that provoked by tuberculin. There was a sense of weakness, shivering, a little fever, 38 to 39° C., the progressive disappearance of the earthy tint of the skin, softening and subsidence of the tumor. The pains are gone, the general state good, lassitude disappeared, sleep restored, the aspect of the neoplasm improved, the patient feels herself much relieved and the inflammation retrogrades from day to day.

Observations of Denissenko, Ivanow, Kraisky and Meyer indicate the employment of chelidonin in gastric cancer, cancroids of the lids and lips, epitheliomas, malign neoplasms and all malignant tumors, external and internal. Many similar reports have been made but few are in such shape as modern science demands.

In gastric ulcer and cancer, enteralgias, cancer of the bowels or larynx and in hepatic tumors, the results of the treatment have been very favorable and rapid, the tumor continuing to diminish, the inflammation arrested, amelioration has been manifest and the cure often appears definitive.

In laryngeal cancer chelidonin has given very encouraging results, when employed locally by lotions and internally. Under its influence the pains of deglutition and the respiratory difficulty vanish and the general condition is promptly and considerably ameliorated.

Spirack collected sixty cases of cancer treated by chelidonine by fourteen physicians, of which thirty-three showed improvement, twenty-seven did not. A remedy that ameliorated more than half the cases is certainly not to be disdained in a disease so desperate. The stomach supports chelidonine very well. Penciling it over the tumor provokes slight brief smarting, while its injection causes sharp, smarting pains, general weakness, chills, fever, from 100.4° to 102.2° F., all which symptoms disappear by the next morning. From the first day of treatment the cancerous complexion disappears, the tumor begins to soften and melt away. At the end of a few days fistulas begin to form around the points of injection. In fifteen to twenty-five days the diseased tissue sharply separates from the healthy, which seems to retreat, and the tumor lessens to one-half or sometimes disappears entirely.

Robinson reported to the Therapeutic Society a case of inoperable cancer completely cured with chelidonine. Kraisky employed it in four cases of cancer of the eyelids and face. In two he obtained amelioration and in two a cure. The evidence of its use in cancer is quite strong.

Chelidonin may be given in very large doses without harm. Houdè advises Gram 0.002 (gr. 1-30) six to eight times a day or twelve times in old cancerous diatheses. It is well tolerated. In gastralgia, enteralgia, etc., when only the calmant and hypnotic effect is desired, the doses need not be so large. For lotions and hypodermic injections he advises 1-1000 solutions.

Dr. John Ketterle, of New York, says: "My first experience was an almost moribund case of cancer of the pylorus, a large tumor being palpable beneath the abdominal walls. Having read of a suggestion (in alkaloidal literature) of injecting condurangin directly into carcinomas, I suggested to the consultant that we try it in this case, with strict antiseptic precautions. He would not consent to this and his influence was all-powerful. He made the same excuse as other physicians make, that they are afraid that it would release too much poison into the system and thus overwhelm it with a cancerous toxemia.

"I did, however, persuade him to let me try condurangin and chelidonine by way of the stomach. The experience here was not a

fair trial, but it seems the chelidonine did ease the pain and brighten the patient for the short period he continued to live.

Case 2. A cauliflower uterine cancer in which chelidonine had no perceptible effect.

"Case 3. Cancer of esophagus near the stomach. When this patient first came under my treatment he could not swallow, regurgitated his food, suffered great pain, was terribly constipated, although he had had no medicine for a few weeks prior. Was passing ribbon-shaped, tenacious, putty-like stools which were difficult to remove even with enema or finger.

"I started him on chelidonine granules, one four times daily, to begin with, gradually increased to sixteen daily (four times four). Used it cautiously, but no bad symptoms were noticed. I had tried to pass an esophageal bougie at various times, but was at first unsuccessful as I was afraid to use force, but had to try something, as he was getting no food into the stomach. Chelidonine was dissolved on the tongue to get its local effect, if any.

The patient soon brightened up, pain was relieved in a few days, and he talked about going to work. It also seemed that the chelidonine had a softening effect upon the stricture, for I was gradually able to get a sound into the stomach. The size of the sounds was cautiously increased until I had a pretty good opening. The patient remained in fair health for a few months after this treatment although he had been under my care only a month; however he neglected himself thereafter, drinking heavily, and when I saw him again he was back to his old condition. He died before I got another supply of chelidonine.

"Case 4. Cancer of the stomach, as indicated by a test of stomach-contents. The patient never vomited, did not even vomit blood toward the end of life, as some do. The tumor, which showed later on, may have been about the colon, pancreas or spleen. I don't know which, but was inclined to think it pressed on the transverse colon very early in the disease, because in this case the stools passed also were ribbon-shaped. Pain was intermittent but intense and resembled attacks of true colic.

"This patient had all kinds of treatment before he came to me. A specialist advised methylene-blue, which treatment was faithfully carried out, but with no encouraging results. As soon as I got another supply of chelidonine I gave him some of the granules and advised eight per day (four times two) to begin with. By some mistake he took sixteen a day (eight times two), which was followed by such immediate and marked improvement that the

patient went back to work after being at home four months, and his family expressed the hope that perhaps it was not cancer. Then it was found that fourteen granules (seven times two) per day acted best. Pain ceased almost entirely, although there always remained a tenderness over the tumor. The size of the latter certainly did decrease, the patient gained in weight and color, and constipation and ribbon stools gave way to regular dark-brown feces. Improvement continued until my two-months' stock of chelidonine granules ran out. He was then put on condurangin, both by mouth and hypodermically. He gradually grew worse and eventually died. Toward the end I resorted to morphine, but it did not act nearly as well as chelidonine in subduing the pain.

"Case 5. In this case the hypodermic injections of condurangin, 1-67 grain each, three in number, at intervals of three days, were given after my supply of chelidonine had become exhausted and the tumor had grown very large. These injections were made with a strong needle through the abdominal walls and into the firm structure of the growth. No improvement or bad results followed, showing that this treatment is not necessarily fatal as my colleagues prophesied, for I ceased the injections fully one month before death ensued.

"Cases No. 3 and 4 passed ribbon-shaped stools, showing a stricture, although in each the stricture was high up. In both instances these stools were of a clay color, which improved under the chelidonine.

"Case 6. Patient sick six years. The intense pain was the only thing that pointed to cancer. According to every authoritative description he had no cancer, nor did it seem probable to me. However he did have coffee-ground vomit (for the first time) one week before he died. During the seven years of his illness nothing gave this patient as much relief as chelidonine. I had this patient about one year, and as he was accustomed to changing physicians every few months, I felt that the chelidonine did act beneficially at least in this case.

"What may we learn from these experiences? I think that chelidonine has a dissolving action on the fibrous structure of the growth. This is possible, and hence we must be prepared for toxemia, which you combat by nuclein. Chelidonine acts like thiosinamin. Perhaps cancer will have to be fought on this plan.

"Let me add that every case that I have here mentioned was positively diagnosed as cancer, which might be guessed by the invariably fatal issue.

"Whatever caused the clay-colored stools in the foregoing cases I do not know, but as chelidonine changed this, perhaps it also acts on the liver as Ellingwood suggests.

"The patient, case No. 4, who had a stenosis of the eustachian tube, complained of buzzing and noises in a slightly deaf ear while taking chelidonine. Perhaps this was due to a softening action."

The hypnotic properties of chelidonine fit it for use in pains of the stomach and intestines, in gastric ulcer, enteralgia, etc. For its hypnotic and specific properties it is recommended in cancer of the stomach. In cancer of other organs it may be given in doses of two milligrams of the pure alkaloid, increased progressively. At any rate it may moderate the spread of the disease and at the same time relieve the suffering. The dose of two milligrams may be given five times a day to begin with, increasing to ten or twelve daily doses, until the limit of tolerance is reached.

CHIMAPHILIN

Standard granule—gr. 1-6, Gm. .01.

Chimaphilin is a concentration from the leaves of Chimaphila umbellata, pipsissewa, prince's pine, ground holly, or wintergreen. The active principles are arbutin, chimaphilin and several others not yet studied. The remedial virtues accredited to this plant are those of arbutin. It has also a volatile ingredient, as the infusion is said to possess a value that is lost in the decoction.

Felter and Lloyd credit pipsissewa with diuretic, tonic, alterative and astringent properties. It increases waste and affects nutrition. It is used in scrofula and in chronic rheumatic and genitourinary affections. It relieves irritation of any part of the genitourinary tract, and improves the nutrition of the affected tissues. Its special field is in genital discharges with debility or scrofula. Cystitis with offensive urine, and urine loaded with mucus, muco-pus or blood, are benefited. Chronic pyelitis is also favorably influenced by pipsissewa, as well as chronic prostatitis, scrofulous ulcers, ascites, strangury, gleet, lithemia, etc.

Specific Indications.—Atony of the genitourinary organs, with lingering disorders, scanty urine, profuse mucus, pus or blood in urine, dysuria with smarting or burning pain, chronic irritation of urethra or prostate, relaxation of bladder walls, chronic prostatitis with vesical catarrh.

Ellingwood says chimaphila aids in restoring the excretory functions to a normal condition and removes irritation of the urinary

tract, lesions of the skin and lymphatic glands, and removes waste matter from the blood, the result of defective metabolism. He finds its field in uricacidemia, dropsy with debility and anorexia, inflamed cervical, mesenteric or parotid glands, dropsy after exanthemata, chronic rheumatism, hectic with nightsweats, secondary syphilis, hematuria, gravel, gout, nephritis, the late stages of typhoid fever with deficient excretion, and mammary tumors supposed to be cancerous. For acute rheumatism he advises a warm infusion to be given till it causes perspiration, and the same applied to the affected joints.

Any virtues not due to the volatile ingredient may be much more easily obtained by the use of arbutin. Like it, pipsissewa blackens the urine.

The dose of chimaphilin is a grain before meals and at bedtime.

CHIONANTHIN

Standard granule—gr. 1-67, Gram 0.001.

Chionanthin is derived from the bark of the root of Chinonanthus Virginica (fringe-tree). The shrub is a native of the southeastern states and its medicinal qualities have been recognized popularly for a long time.

The eclectics regard this remedy with favor and it is unquestionably a most valuable hepatic stimulant and alterative. Chionanthin is aperient, diuretic, febrifuge, cholagog and purgative. Its tonic and alterative action is also marked if dosage is continued. In fact, it is as a continued remedy for chronic engorgements and sluggish liver that it has most value. In full doses (2 to 5 grains) it has a pronounced cholagog action and may be given in extreme conditions with podophyllin. But its main utility is as an alterative hepatic in jaundice, bilious conditions and catarrhal states of the bile-ducts. Then it should be given in doses of from gr. 1-6 to gr. 1-2, preferably after meals, three times daily. In a few days the skin clears, the patient feels brighter and his appetite returns. It seems to have a specific action in overcoming catarrh of the ducts, promotes the flow of bile and prevents the formation of calculi.

In any acute congestion of the liver this is the remedy of choice and should be given in full doses followed by sodium phosphate or other saline laxative. The jaundice of childhood rapidly yields to this remedy as does that of pregnancy. In all malarial conditions it is to be thought of and may be given during either the chill or fever with equally beneficial results. The author has found it in

doses of gr. 1-3 three times daily unequalled for restoring to healthy activity the livers of sedentary workers. It may be combined with iridin, euonymin, leptandrin or podophyllin. It is a remedy which should be more used than it is.

King recommended chionanthus in bilious and typhoid fevers, obstinate remittents, and as a tonic in convalescence from exhaustive diseases. The active constituent is a resin. It improves the appetite, aids digestion, promotes assimilation, never causes catharsis but has induced ptyalism. It has done well in treating mercurial cachexias, scrofula, and as an adjuvant in syphilis. Felter and Lloyd say: "If there is any one thing true in specific medicine it is that chionanthus has a decidedly specific action in jaundice." Goss excepted that dependent on gallstones, but Scudder praised it highly here, giving it during the paroxysm and to prevent recurrence. Hypertrophy of the liver, hepatic inflammation, portal congestion, are speedily relieved by it. Dull, heavy pain in the right hypochondrium, a sense of fullness and weight, deep-seated tenderness on pressure, hectic flushes, light colored feces, sometimes diarrhea with frothy, yeasty stools, urine scanty and red, with jaundice, call for chionanthus. The patient may writhe in pain, finding no relief in any position. In dyspepsia with hepatic complications, irritative states of the stomach from high living, and alcohol, chronic duodenitis and catarrh of the bile ducts, infantile dyspepsia, rheumatism with hepatic soreness and jaundice, as a tonic to the chylopoietic viscera in general debility, and in intestinal dyspepsia with jaundice, thin watery yeasty stools, with previous abdominal distention, chionanthus finds its place. It is often useful in chronic splenitis and nephritis; pancreatic disease, glandular disease with imperfect waste, uterine and ovarian congestion with hepatic symptoms. If there is fullness and bearing down of the pelvic viscera and a desire to frequently evacuate the rectum, add helonias. In female disorders gelsemium, macrotys and pulsatilla may be also indicated. In all cases it is essential that other prominent indications should be met to secure the best effect from chionanthin.

Specific Indications.—Dirty, sallow skin, expressionless eyes and tender liver; icteric hue with or without pain; hepatic colic, intense pain from liver to umbilicus with vomiting and great prostration; pain in epigastrium and right hypochondrium like colic, sometimes extending to abdomen; jaundice with itching skin, thin, light, watery stools; tympanites, colic with green stools; urine staining clothes yellow.

CHROMIUM SULPHATE

Tablets—gr. 4, Gm. 0.25.

The internal use of chromium sulphate as a medicine began with a paper presented to the American Therapeutic Society at its meeting of 1908, and published in the *Monthly Cyclopedia and Bulletin* for September of that year. The writer, Dr. Louis Kolipinski, had introduced this remedy to the same society six years previously, but it had not elicited any attention. Since the first paper appeared there had been the revival of interest in drugs which the active principle advocates had inaugurated, and the second paper was taken up by them. During the three years following enough reports have been made upon chromium to enable us to form some idea as to its merits from the clinical standpoint.

Kolipinski claimed that being non-toxic chromium sulphate could be administered in doses of eight grains three or four times a day to adults, and that "thirty to forty grains at one time result in no unusual sensations except a very mild vertigo or lightness in the head." He advised a 4-grain tablet or pill after meals. Sometimes the unabsorbed residue colors the feces. No unpleasant by-effects were noted in patients who had taken the drug continuously for four or five years.

The diseases in which he had found chromium sulphate successful were mammary cirrhosis, castration (?), menopause, functional impotency in men, chronic alcoholism, nervous vomiting and that of pregnancy, neurasthenia, locomotor ataxia, exophthalmic goiter and the migraines. In neurasthenia, ataxia and goiter the results were speedy and striking. In neurasthenia he pronounced it the only drug that was curative. "In exophthalmic goiter the rapid pulse and churning motion of the heart are invariably reduced to nearly normal; the pulse remains so. The nutrition of the body is bettered, the trembling ceases, likewise the state of nervous erethism and irritability. The bulging eyes and struma recede slowly." Most of his cases were old, neglected or mismanaged, and fresh ones yielded prompt results. Ataxia he pronounced curable by chromium; the more recent the case and the earlier the remedy was begun, the quicker the result. The pains and crises succumb. In first-stage cases all symptoms vanish and do not reappear. In the atactic stage the incoordination is permanently removed; the staggering, unsteady hand motions, vesical and rectal sphincter pareses disappear. In the third stage most decided improvement is possible; the patient being enabled to walk without

crutches; he is restored to the first stage and this also recedes. Advanced stages either subside or cease to advance.

Among maladies more recently found amenable to chromium sulphate he cites chronic prostatic enlargement in old men, a symptomatic cure being won in a few months, the vesical irritability subsiding, the sleep being restored, the catheter laid aside, the cystitis remaining unaffected. Chromium retards the growth and reduces the size of uterine fibroids, especially in young women.

These effects the writer attributes to stimulation of the absorbents, chromium thus ranking with thiosinamin and fibrolysin.

To test the alleged innocence of chromium sulphate we made some experiments in our laboratory. Two full-grown healthy guinea pigs were selected; to each was given chromium sulphate in doses rising to 12 and 16 grains on the third day. The first evidences of disturbance then appeared, six hours after the dose; as a fall of temperature to 97° and 97.2° respectively, diarrhea, dyspnea, and in the one that received the larger dose, paresis. Both died before morning. Assuming the same degree of toxicity for men, an average man would require 900 to 1500 grains to cause death. Some digestive irritation would be caused by smaller doses, but the daily maximum of 50 grains is well within the limits of safety.

Many reports have been received on this remedy.

G. T. Fuller, Mayfield, Ky., concludes that "chromium sulphate spends its force entirely upon the nervous tissues, and is not only a tonic to them, but a food as well. If not a food in fact, it so stimulates the nerve tissues that they appropriate to themselves nourishment from the blood plasma, in the way of phosphorus, magnesia, and potassium cell salts, and other material necessary to their normal health and functional activity. The drug is indicated in the functional wrong of any organ where the organ is due to lack of nervous tone or impoverishment of the nerves supplying same. It is indicated in a few structural wrongs in addition in organs or tissues extra to the nerves themselves, as for instance in goiter and exophthalmic goiter.

"Chromium sulphate has never failed in a single instance to at least alleviate the symptoms of prostatic hypertrophy, and in most cases to effect a cure; and its action in bringing about this better condition of affairs is exactly the same as in goiter—it inhibits the blood through the hypogastric plexus, and by that means brings about a gradual involution of the prostate gland. It not only reduces the size of the gland, which, from mechanical pressure, paralyzes the cut-off muscle of the bladder, but, by its action through the

nervous system it so tones those muscles as to enable the old man to retain his urine a reasonable time and pass it at his pleasure."

Dr. W. H. Cowan states that an epilepsy subsided during three months' use of chromium sulphate. A uterine fibroid shrank in the same period of its administration, with concomitant improvement in the nervous condition. A cure was secured by its use in nervousness and hysteria from overwork while preparing for a wedding.

Dr. C. O. Rice, of Mexico, found it successful in a case of exophthalmic goiter, marked; and in neurasthenia, "many, many cases of migraine, and one of locomotor ataxia, the last with marvelous results."

Dr. S. J. Ross, of West Virginia, succeeded in curing an enlarged prostate by three months' use of chromium sulphate.

Dr. R. J. Boynton, of Massachusetts, cured two cases of neurasthenia and one of amyotropic lateral sclerosis, well-advanced; and in ataxia, neuritis and neuralgia it proved curative.

Dr. C. E. Henry, of Minnesota, reports two cases of ulcerative proctitis cured. He also found this salt useful in early pulmonary tuberculosis.

Dr. A. D. Kurtz, of Virginia, gave it for ataxia with aphonia, finding it beneficial only for the latter. Sixty grains a day caused nausea. Aphonia from disease of the vocal cords was benefited only temporarily.

Dr. Kenny, of Idaho, got from it surprising results in the prostatic troubles of old men.

Dr. L. B. Allen says, in *The Medical World*, that he found it useless in prostatic enlargements, but the best of aphrodisiacs.

Dr. J. W. Fyfe, in *The Eclectic Review*, pronounces it useful in ataxia, exophthalmic goiter and prostatic enlargement.

Dr. J. A. Burnett, of Oklahoma, tried it for an old man with cystitis, finding the drug caused diarrhea and severe griping in the lower rectum, but did not relieve the frequent urination or the burning during urination.

Dr. J. W. Dill, of Illinois, succeeded with it in enlarged prostate and in uterine fibroids.

Dr. H. M. Arthur found that it cured ordinary goiters in 90 days, an exophthalmic goiter in 60 days, another exophthalmic case in 42 days, a third case was better after 30 days' treatment, a fourth much better in the same period, and an enlarged prostate no better after 60 days.

Dr. Waugh gave a lady with severe and intractable migraine two tablets, an hour apart, taken on an empty stomach; with slight

relief after the first dose but vomiting and no relief after the second. This was of course no test of its efficacy, which is as a remedy for the intervals rather than for the neuralgic paroxysms.

While chromium sulphate is still *sub judice*, it is worthy of extended trial.

CICUTINE

Standard granule—gr. 1-134, Gm. .0005; cicutine hydrobromide, gr. 1-67, Gm. .001.

The use of conium, celebrated in antiquity, has fallen into oblivion in most countries, on account of the uncertainty and general worthlessness of its galenic preparations. Dragendorff found in the leaves and fresh bark 0.0466 to 0.094 percent of cicutine; in dried leaves 0.26 percent, and in seeds gathered before maturity 0.766 percent. Holmes found no toxic properties in the Scotch hemlock. Close could isolate only 0.0003 percent of active principle from the ordinary dried leaves of the pharmacy. Von Schroff observed no toxic results from doses of 30 to 60 grains of the extract given to rabbits. At Dixmont we used the extract as a pill excipient in 1872. Such observations suffice to condemn the remedy as far as concerns the galenic preparations and the crude plant.

Burggraeve found the hemlock of the shops adulterated with many other species of cicuta, and other unrelated plants, from which great irregularity in the action of the preparations resulted, some producing terrible effects and others none at all. Von Schroff said that the yield of cicutine varied with the age of the fruit. Smith found that the leaves lose very rapidly the most of their efficacy. Bouchardat pronounced the hemlock a dangerous plant. The conicine of commerce is impure and contains methylconiine. The extract of conium leaves has no action and may be eaten without inconvenience (Bochefontaine and Mourrut). Lepage proved that the root gathered in March had but an extremely minute trace of alkaloids. That gathered in May was about the same, the plant being then in full leaf. So also in June, but in September the roots of plants of that year were richer than those of the preceding. The fruits proved especially rich in alkaloids, which could not be detected in oils prepared from roots reduced to a pulp, but were found in the oil from the leaves, stem or fruit. The bad quality of the preparations is dependent on the variable quantity of alkaloid in the plant, its great volatility and its tendency to spontaneous decomposition.

Cicutine is a liquid, lighter than water, readily decomposing in air, and volatile. It is more soluble in cold than in hot water;

and is quite soluble in alcohol, ether, chloroform, acetone, benzole and the essential oils. The alkaline reaction is strong, even replacing ammonia. The salts of cicutine are quite permanent and free from objection, and these are preferable. The hydrobromate is in the form of small colorless rhombic prisms, resisting the air, soluble in water, containing 60.7 percent of cicutine. It may be used subcutaneously, while cicutine is irritant.

Physiologic and Toxic Actions.—To the mucosa cicutine is irritant, but solutions applied to the skin produce anesthesia. In ancient times the hierophant presiding over the Eleusinian mysteries is said to have applied conium to the genitals of initiates to render easier the fulfillment of vows of chastity. In the eye the first irritation is great and the subsequent anesthesia correspondingly profound.

Cicutine is eliminated by the urine and the lungs, and in part broken up in the body.

The predominant action of cicutine is paralysant, at first of the terminal extremities, then of the trunks, of the motor nerves. At first limited to the voluntary muscles, it extends to those of respiration, the left heart, next to the diaphragm, and finally causes death by asphyxia, the preceding dyspnea accompanied by clonic spasms. The heart-action remains long unaffected if deoxidation is prevented by forced respiration. Consciousness remains unaffected to the last. There is probably a special action on the spinal centers, since reflex action is lost before irritability of peripheral nerves ceases.

One-fourth of a drop of cicutine taken in the mouth of a healthy man causes a sense of burning to the tongue, slight constriction of the throat, flow of saliva, nausea and vomiting, general malaise and heat of the head. A drop produces alarming symptoms, such as vertigo, impossibility of fixing the thoughts or the attention, somnolence, very marked malaise, ocular troubles, dilated pupils, alterations of touch and hearing, tremors, weakness, gait uncertain and vacillating, cyanosis, cold sweats, finally spasmodic muscular contractions when the muscles are forced to move. The pulse is small and weak, a slight primary rapidity being soon followed by slower pulsations.

Burggraeve reports the following effects when taking cicutine: Tendency to repose and slumber, without fatigue, quite different from that of morphine; the waking calm, without headache; softening of the pulse; notable diuresis and diaphoresis. It is evident how cicutine calms the pains of cancer and restores the forces by sleep.

Eulenberg mentions a sense of weakness and vertigo as following a subcutaneous dose of gr. 1-67 but double this dose later did no harm to the same patient.

In warm-blooded animals the effects of cicutine are manifested a minute or two after taking, by general paralysis, beginning sometimes with the anterior, sometimes with the posterior extremities; the respiration at first irregular is arrested, the heart continuing to beat for hours. If the dose is not fatal the animal recovers within twenty-four hours. Ligation of the iliac artery prevents paralysis of that limb. The only convulsions occurring are the clonic ones with asphyxia. Fibrillary muscular contractions from the first are probably due to a primary excitation preceding the peripheric motor paralysis. During the paralytic period the sensorium and sensation are unaffected.

Cicutine exerts its effects on the nervous centers, since ligation of all the vessels of the extremities does not prevent the diminution of reflex sensibility. The psychomotor centers appear, however, to be only affected secondarily, and from the deprivation of oxygen or the alteration of intravascular pressure. The lachrymal, salivary and renal secretions are increased by cicutine, but Prevost denies any direct influence on the sensory and secretory nerves. Jolyet and Pelissard have demonstrated the paralyzant action of cicutine on the pneumogastric nerve-ends, showing very quickly and after doses too light to paralyze the motor nerve-ends.

Previous to its sedative action cicutine exercises a powerful incitative influence over the nervous system, in small doses; facilitating digestion and assimilation, and augmenting the urine and sweat (Harley). It seems to act directly upon the motor and sensory nerves (Koelliker, Funke, Pelvet, Damourette, Gubler, Ruatta), and Laura claims also a direct and specific action on the cerebro-spinal centers, and possibly also on the nerves controlling the iris. Harley claimed a special control over the corpora striata. Laura found it exert an active and evident power over the glandular apparatus, which it even atrophied after long usage. According to Burggraeve it calms sensibility and contractility, calms and regulates the circulation.

The intravascular pressure and the animal heat are increased, even after medicinal doses. The respiratory movement in grave poisoning is at first accelerated and convulsive, then retarded. The respiratory mechanism is not disturbed by light doses, which cause only irregular and paretic rhythm. Mydriasis is a pretty constant sign; rarely the opposite effect is seen.

Intestinal peristalsis persists even after death.

Ihmsen reported changes in the blood, but this is denied by Huesemann.

Binz reports an interesting case of poisoning with half an ounce of the fluid extract of conium, in a young woman of feeble constitution. Twenty minutes after taking this dose she was seized with nausea and vertigo; she let fall what she was holding, and could not walk. She was put to bed. The pulse rose to 120 but soon became calm. She was calm but could not execute the least motion of her arms or legs. An hour later the paralysis had extended to nearly all the muscles. The eyes were closed, the pupils dilated, the brain perfectly clear, calm but active. Asked to open her eyes, she could not move the lids. Pulse and respiration normal, heat of the skin natural. After an hour she could open her eyes, and in three hours motion was reestablished. Next day there were only slight pains in the muscles of the legs. In this case the heart and brain remained unaffected; but if still larger doses were taken paralysis of the diaphragm would follow, with cyanosis and its effect on heart and brain.

Imbert-Gourbeyre spoke of delirium and convulsions from hemlock, but he probably used impure preparations.

Sollmann says that the alkaloid of commerce consists of a mixture of four, which differ mainly as to their relative strength. As they decompose very rapidly the commercial preparations are often entirely inactive. The hydrobromide is the most stable. Cicutine closely resembles nicotine, standing between it and curare. It paralyzes motor ends and ganglia, depression of the central nervous system forming the most prominent feature of its toxic action on man. The paralysis is ascending, reaching the tongue while consciousness is unaffected. Convulsions may appear, as the cord is little affected. Death is due to respiratory paralysis. Its action would justify its employment for strychnine poisoning or other tetanus, chorea, whooping-cough, torticollis, etc. "It would possess the advantage over curare that it acts on the seat of the disease, centrally as well as peripherally. The hydrobromide deserves the preference."

Since Ladenburg in 1886 produced cicutine synthetically it has been re-tried with the chemically pure substance thus secured, and the foregoing account of its actions practically confirmed. Respiration was first accelerated, then retarded. The blood-pressure rises at first, then sinks to normal, and only after large doses does it fall below normal. Cicutine paralyzes the terminals of the in-

hibitory fibers of the pneumogastric without preliminary excitation. The cessation of breathing is not due to paralysis of the respiratory center but of the motor terminals in the respiratory muscles, especially those of the phrenic nerve.

Synergists.—Van Renterghem names morphine, atropine, hyoscyamine, lobeline, curarine, veratrine and aconitine, all which diminish or abolish muscular irritability, motor nerve conduction, and the excitomotor force of the spinal cord.

Antagonists.—Strychnine, brucine and picrotoxin figure here. This antagonism is only relative, since strychnine increases the reflex irritability of the cord, while cicutine reduces the excitomotor force of the medulla.

Tannic acid and potassium iodide are chemical antidotes.

Therapeutics.—Van Renterghem says the Germans, who have no active preparation of conium, find it useless; the English, who possess an active agent in succus conii, find it of positive value.

In whooping-cough its favorable action is comparable to that of atropine. Applied locally it lessens exaggerated sensibility and extinguishes the pain of neuralgias and of various tumors, even of cancer.

Binz found cicutine useful in the tetanus of strychnine, in blepharospasm, and in external neuralgias.

The sedative effect exerted by cicutine upon the spinal cord indicates the use of this agent in all cases characterized by tonic convulsions, contractions or tetaniform rigidity, as well as in whooping-cough, rabies, traumatic and spontaneous tetanus, and in poisoning by any of the strychnine group. Pereira states, however, that in spite of the cessation of the convulsions, death seems to be hastened by the cicutine. Its antidotal value must be decided by clinical observations.

Cicutine is not only hypocinetic, but it is stupefying or anesthetic, and therefore useful in affections eminently dolorous. But it is in the hyperesthetic and spasmodic affections of the respiratory apparatus, which serves it as a way for elimination, that cicutine renders great services. To avail ourselves of its volatility it must be given free, in alcoholic solution, diluted.

Since the day of Storck, hemlock has been employed empirically for ganglionic and visceral engorgements, and for cancer. The moderns have accorded the same powers to the alkaloid, but its real benefits are limited to relief from the pains and spasms. In scrofulous ophthalmia with excessive photophobia and palpebral spasm, Fronmueller and Mauthner applied it with success. In

inoperable mammary cancer with axillary involvement, von Schroff reported the cure of very extensive carcinomatous ulcers and the arrest of the malady after the employment of conium for many consecutive weeks.

Dujardin-Beaumetz said that while resembling curare it differed in also sedating the pneumogastric, and causing anesthesia. He was led to use it in perturbations of this nerve, and of the nervo-motor system. With potassium bromide it should give good results in convulsions, especially the reflexes emanating from the vagus, convulsive cough, asthma, whooping-cough, hiccough, dysphagia, vomiting, spasmodic bronchitis and laryngitis.

Stewart and Corry cured with cicutine two cases of traumatic tetanus. Welch and Harley cured choreics with it.

In the convulsions of infancy, in tic douloureux, it should be of value. As it accelerates the pulse (Casaubon), lessens arterial tension (Pelvet), perturbs the system and the hematic functions (Casaubon), which gives the key to its resolving action, cicutine should exhibit these effects when pushed to sufficient dosage.

Huesemann considers it useful for muscular spasms of peripheric origin, for angina pectoris (Erlenmeyer), and the obstinate and fatiguing cough of phthisis (Nega). As an antidote for strychnine, picrotoxin and carbolic acid, cicutine has not succeeded. It is not as anodyne as morphine. In cardialgia it often fails, except when accompanying functional affections of the liver (Reil). Locally it relieves the pain of dental caries.

It answers marvellously for blepharospasm and photophobia; and Schultz recommends it in place of curare for localized spasms.

Van Praag thinks it contraindicated for cachectics and those threatened with paralyses. Reil advises to avoid large doses in neuralgias in chloroanemics, and says it causes vertigo in the well nourished and plethoric, and those of irritable temperament. It has failed in tetanus and hydrophobia.

Cicutine is indicated with the mydriatics as an antispasmodic, for hyperesthetic and neurosic pains, irritations of the spinal cord, and painful spasms of the sphincters. It calms the lancinating pains of cancer without exercising any control over their course. In spasmodic coughs it sedates while favoring secretion. It procures calm sleep, without heaviness on waking, a valuable power. As an antaphrodisiac it is of value, combined with camphor monobromide. It also controls hysteria at the height of the paroxysm.

In cutaneous hyperesthesias, pruritus, angina pectoris, it has had good success. In tuberculous meningitis it lowers the fever and

sedates the excited brain. In all maladies of infancy with hyperesthesia it may be employed with success.

The best preparation is the hydrobromide, the dose gr. 1-67, to be repeated as often as the conditions indicate, every ten to twenty minutes in acute or painful affections, or three granules every four hours in chronic forms of disease.

Subcutaneously the hydrobromide may be given in watery solution in doses to suit.

Locally, Van Renterghem recommends a solution of gr. 1-12 in 1 1-4 to 3 3-4 drams of weak alcohol, for application to the skin or mucosa in pain. For blepharospasm and scrofulous glands Mauthner advises gr. 1-12 in 1 1-4 drams of sweet almond oil. This serves as a collyrium. Or we can use a solution of gr. 1 1-2 in 150 minims of weak alcohol, or a suspension in mucilage. But cocaine has replaced cicutine here.

As a hypnotic cicutine may replace the bulky synthetics so energetically exploited of late. There is not one of them as easily given, or so certain to relieve the irritability that prevents sleep; while cicutine has an anodyne power that excels all of them; and while not equal to that of morphine it can be used in many cases where the latter is not needed, besides being free from the physical and moral objections accruing to the use of all opiate derivatives. When this use of cicutine is fully comprehended it will become one of the stand-bys of our practice.

In cancer a few doses of an inert or uncertain preparation have been given, and on the certain failure resulting the drug has been condemned as useless. Give it internally and apply it locally in full doses, and see what the ancient repute of hemlock is worth when administered with modern thoroughness. We cannot afford to lose anything that will assuage the atrocious pangs of cancer, or that has a possibility of effecting a cure. The hydrobromide should also be injected into the substance of the tumor, in doses beginning with gr. 2-67 and rising to full toleration. The use of the alkaloids necessitates a restudy of applied therapeutics.

Laura pronounces the effects of cicutine in glandular engorgements marvelous, without the least inconvenience, as in those of the vast lymphatic apparatus, adenomas internal or external, strumous engorgements of the bronchial and abdominal glands, subcutaneous scrofulous adenopathies, mild engorgements of the liver and spleen, deforming and alterant gout, so important as producing grave respiratory and circulatory disorders. "If we can not believe cicutine capable of curing really cancerous affections, or of

resolving cancerous degenerations, it serves at least to diminish the part of the tumor capable of resolution, the concomitant engorgements and obstructions, secondary and collateral. If it can not directly ameliorate the diathesis, in small doses by inciting the digestion and assimilation, by its happy influence over the organic exchanges and by its hypnotic action, it can be utilized as an excellent modifier and an indirect restorer of the organic forces of life." (Laura). Besides this it relieves the terrible pains of this malady, and by this conserves the vitality, preventing the pain, the loss of strength, the malassimilation, the insomnia, the disorder of nutrition, the febrile element, and the discouragement, all which hasten the end. In such conditions when we are depressed by our inability to cure, cicutine appears as a veritable benediction, a remedy a thousand times more efficacious, prompt and well tolerated than the most vaunted calmants, without excepting any of the famed alkaloids from opium (Laura). "But—one must not depart from the rules of right dosage, for huge doses at once or too closely repeated may ruin the life of the nervous centers and the assimilative and vegetative life, and advance the final ruin of the organism."

Burggraeve employed cicutine in affections of the spinal cord, with reflex movements; in intercostal neuralgias, angina pectoris, dental pains, otalgia, and to relieve cancer pains; as an antispasmodic instead of atropine, as an excellent calmant for spasmodic coughs; as a hypnotic to secure calm sleep; and as an antigenesic in hysterias threatening paroxysms. Laura suggests that its long-continued use will modify the scrofulous diathesis itself, employing small doses with occasional intermissions. It is indicated in spasm of muscular fiber, smooth or striped; in bronchial spasm, laryngospasm, spasm of the hollow viscera and their ducts, the hyperesthesia of asthma and of whooping-cough, angina pectoris and even in acute mania. Here a marked tolerance is observed for this remedy. Here Laura recommends cicutine hydrobromide in small doses at short intervals, during the paroxysm with acute pains showing predominance of the spasmodic element.

Cicutine does well in neuralgias, especially when they have the character of a fixed pongitive pain, and still more in visceralgias to which it puts an end, especially in the acute stage. Exercising a direct action on the intercostal nerves it relieves their neuralgias; and Burggraeve found it of extreme efficacy in certain neuropathies, symptomatic of endothoracic phlogoses. It relieves thus the pains of herpes zoster.

For all the uses of cicutine the hydrobromide is preferable. It does not decompose readily and has no disagreeable odor. It agrees well with the most delicate stomach. Bochefontaine and Tinya Kian pronounced it more active than pure cicutine. Burggraeve advised it for tuberculous meningitis with the characteristic cry. Subduing the fever and sedating the brain without constipating like morphine, it could be employed in all maladies of infants with hyperesthesia, without danger. Martin-Damourette and Pelvet thought cicutine could prevent, arrest in the incipiency and prevent the development of the neoplasia by which the great diatheses reveal themselves—the dartrous, rheumatismal, scrofulous, perhaps the cancerous, combating these hyperplasias in the formative stage. Harley recommended it in choreas, epilepsy, and spasmodic contractures of the orbital muscles, and even in obstinate photophobia. Gonzales, Echeverria and Macdonald used it with success to calm the nervous irritability and relieve the depression of the forces so common with epileptics. Hufeland employed hemlock in spasmodic dysphagia, Meyer in spasmodic bronchitis and laryngitis. Hailly cured a rebellious orthopnea with cicutine hydrobromide. Tinya Kian's studies revealed the ease with which the organism becomes accustomed to cicutine, its prompt elimination which prevents all danger of cumulation, the stability of the hydrobromide, its energy greater than the pure alkaloid, its tolerance even in large doses, its elimination mainly by the pulmonary and cutaneous surfaces, and that nursing infants are not incommoded by cicutinized milk; while the smallest infants support the hydrobromide very well. He employed it in coughs, bronchial, phthisical, nervous and others; in whooping-cough, epilepsy, neuralgias, arthralgias, all nervous hyperesthesias, chorea, convulsions, tremblings, and even in tetanus.

As a sedative to the motor nerves and of the reflex function of the spinal cord, cicutine has a definite indication. Many cases show spinal irritability and exaltation of the reflex excitability. The indication is to ascertain and remove the cause, such as autotoxemia; and this has attracted most attention; yet the power of cicutine is not to be despised. Ganglionic excess calls for it, from whatever cause. In many cases of mental perturbation cicutine has proved highly useful. Shaller has called attention to its value when the patient fears the coming of insanity, or actually shows evidences of mental aberration. Also in the nervous disturbances incident to the menopause, it has proved salutary. In fact, the whole group of socalled hysteric affections is speedily controlled by cicutine. These

generally show a state of morbid excitability, an exhaustion of neural force, and consequent inability to withstand the numberless petty irritations of life without an explosion of temper or emotion. Here cicutine is more efficient than valerian, and pleasanter to administer. The two are synergistic, and may often be combined with advantage.

In true asthma cicutine is better than in the asthmatic attacks incident to chronic pulmonary or bronchial maladies, where the sedative effects of the drug on the respiratory apparatus may not be advisable. Stimulants like strychnine or aspidospermine will then do better.

Cicutine has not been given sufficiently in motor spasms like chorea and epilepsy. Alone it may be insufficient, but it aids other remedies greatly, and should form part of the treatment. Muscular twitching with cerebral fullness sometimes prevents sleep, and here it is difficult to find so admirably suitable a remedy as cicutine.

Dysmenorrheas of the spasmodic variety, and those connected with pelvic inflammations, are well controlled by cicutine, alone or in combination.

The fact that cicutine partially controls the effects of strychnine in toxic doses, though neither prevents the fatal result from the other, well illustrates the parallel or coincident action of apparently antagonistic agents.

Now that a uniform and effective form of this remedy is available, we may expect to see its therapeutic applications multiplied in the near future. It is well worth further study and trial.

CINCHONIDINE

The writer once undertook to demonstrate the chlorine test for quinine before his class. The "quinine" was placed in a test tube, chlorine water and ammonia added, and—no green color ensued! As long as quinine costs more than cinchonidine, much of the latter will be sold as true quinine.

Does it matter? The effects of cinchonidine, physiologic and therapeutic, are practically identical. The dose is about the same. Some stomachs find cinchonidine easier to bear than quinine. Possibly when the alkaloids that thus closely resemble each other are carefully studied, in the light of modern science, we may learn why it pleased the Creator to produce several of these bodies instead of one. Minute differences will be discovered rendering each more accurately suited to certain conditions than the others. But this

has not yet been done. For the present we must refer the reader to the chapter on quinine.

Cinchonidine is very slightly soluble in water or in ether, more so in alcohol. The sulphate is soluble in 100 parts cold and 4 parts boiling water, in 71 parts alcohol, easily in acidulated water. The hydrochlorate is soluble in about 40 parts cold water. The tannate is a white tasteless powder, and possibly forms the basis of the "quinine" chocolates in the market. It has been recommended in diarrheas in doses of five to fifteen grains for adults.

CINCHONINE

The value of cinchonine lies in its insolubility. Requiring over 3,700 parts of water, cold or hot, to dissolve it, this salt has been repeatedly exploited under the name of "tasteless quinine." It is only after being held some time in the mouth that the bitterness is developed. For children it may be given mixed with powdered sugar, and chocolate or cinnamon, without difficulty. This slow solution also renders cinchonine less apt to irritate the stomach. There is practically no available solvent for cinchonine, as it requires 371 parts of ether, or 400 of chloroform. The best solvent is a mixture of chloroform and alcohol. Even the sulphate requires 70 parts of cold water, 14 parts of boiling water, 6 parts of alcohol or 60 of chloroform. It is insoluble in ether, but readily soluble in acidulated water.

Sollmann says that with cinchonine and cinchonidine the stage of stimulation is said to be more marked than that of quinine, since these produce convulsions. These are epileptiform in character. This action is slight, and is more marked with cinchonine.

The iodosulphate of cinchonine is known as Antiseptol. It is a powder used instead of iodoform, and contains 50 percent of iodine.

The therapeutic uses of cinchonine are those of quinine.

COCAINE

Standard granules—gr. 1-134, Gm. .0005; gr. 1-67, Gm. .001; gr. 1-12, Gm. .005.

The leaves of the coca plant have long been used in South America as a means of enabling the user to withstand fatigue and the lack of food. The leaves are made into a masticatory. It is said that incredible journeys are made by the Peruvian Indians while chewing these leaves. When the Spaniards conquered Peru they found the Incas regarding the coca plant as sacred, and immediately

proscribed it, inflicting the death penalty on any native on whose premises it was found growing. For centuries coca attracted no attention, though Isaac Ott, who investigated it a number of years ago predicted that it would one day fill a great place in therapeutics. But it was not till Koller discovered the anesthetic action of cocaine that the medical world awoke to a realization of the value of this drug. The keen commercial instincts of the nostrum venders aided in the exploitation of coca, and a whole noxious brood of wines and other preparations appeared. Since that time the use of cocaine as a habit drug has become so extensive that some states have been compelled to legislate against it, and to regulate its sale more closely than the deadliest poisons.

In fact, when one realizes the harm done by this agent it seems as if there were wisdom in the Spanish regulations. In Peru inveterate consumers of coca are known as coqueros, and are recognizable by their unsteady gait, lax yellowish gray skin, lack-luster eyes surrounded with brown rings, tremulous lips, incoherent speech, stupid and apathetic condition. They are suspicious, hesitating, false and cunning. The signs of old age appear before midlife, and if they survive, imbecility results. Excitation of sexuality with loss of self-control makes it doubly dangerous.

Physiologic and Toxic Actions.—Prolonged use of moderate doses of coca lessens the salivary secretion, and lowers sensation in the mouth, esophagus and stomach; causing weakness in the legs, dilated pupils, irregular pulse and respiration, higher temperature, a dreamy state of the mind, disturbed sleep, aphonia, unsteady gait, pleasant or frightful hallucinations, and delirium. These are especially evident after a coca debauch. Exhaustion and depression do not follow such a spree.

Notwithstanding its general use as a local anesthetic, the physiologic action of cocaine is not well comprehended. Schroff observed that it gave rise to vertigo, lassitude, weakness of hearing, enfeeblement of memory and incoordination of thought. Ploss, in a non-mortal poisoning case, noted somnolence, colicky pains, obstinate vomiting, vertigo, collapse, anemia, a sensation of burning and intense thirst. Experimentation shows that cocaine exerts an action analogous to that of cannabis indica, and that it is a narcotic, exercising a direct action, primitive and stimulant, upon the brain (Fronmuller, Tarchanov, Ploss.) Von Anrep and Nikolsky first announced that cocaine is mydriatic. It at first stimulates the nerve centers, then the highest psychomotor cells of the brain, later the bulb and finally the spinal cord.

In feeble doses cocaine excites and stimulates the functions of the stomach, possibly those of the liver. In somewhat larger doses it suppresses the sense of hunger and thirst, probably by a direct anesthetic action upon the gastric nerve-ends. The secretion of saliva then increases largely. Cardiac action and vascular tension are augmented after a slight preliminary depression.

Cocaine induces a general sense of well-being and of nervo-muscular power, rendering the taker capable of sustaining more fatigue. It at the same time augments the excitability of the sensory nerves, of which it is an indirect calmant and sedative. This renders it effective in neuralgias. There is not yet complete accord as to its action. Some with Mantegazza believe that cocaine diminishes the phenomena of oxidation and lessens the waste of the tissues, while others with Moreno hold that on the contrary it accelerates waste and thus lowers the body weight. The one point on which all agree is the anesthetic-analgesant power of cocaine, and upon this one quality its therapeutic use is based.

Friend obtained from cocaine the same results Mantegazza had secured from coca—a general sense of well-being, the pulse fuller and larger, the facility for bodily and mental work increased as well as the resistance to fatigue. He praised cocaine as a stimulant in cases where there had been excessive work, in cachexias, alcoholism and morphinism, and in asthma. As an aphrodisiac cocaine might be of service, and also in disorders of stomach digestion.

The whole central nervous system is affected by cocaine, which acts directly on the nerve cells without affecting the circulation. The increase of reflex excitability, the superactivity of the circulatory and muscular systems, are evidences of the excitation of the centers at the base of the brain. Generally the stimulation of cocaine is followed like that of caffeine by a return complete and without transitional states to the normal state. Enormous doses cause an intervening stage of weakness and paralysis. Toxic doses by the mouth are required to dilate the pupils though small ones applied locally accomplish this readily.

Von Schroff says that after an initial acceleration there is slowing of the respiration. The pulse is hastened by medium doses, retarded by maximal doses. The cardiac fibers of the pneumogastric lose their excitability after small doses and are paralyzed by medium doses. The rapid pulse is therefore as with atropine due to paralysis of the inhibitory nerve. Medium doses increase vascular tension, large doses lessen it rapidly. The surface heat is

augmented, while the central heat falls half to one degree Cent. From the moment the subject enters the convulsive stage the temperature as taken in the rectum rises above normal.

Rossbach says the striated muscles are unaffected. A momentary increase of intestinal peristalsis with ischemia of the intestinal walls is quickly followed by a notable diminution of motion, dilatation and venous congestion. Mucous secretion and saliva are lessened.

No constant effect on the renal functions has been determined.

In fatal poisoning, death is due to respiratory paralysis. The heart continues to beat for some time after death.

Von Anrep made some experiments to determine how far coca replaced food, and found that death by starvation occurred as quickly when coca was taken as without it. The runners who under its influence go long distances without food make up for it by gorging afterwards. But the weight of opinion favors the view that cocaine aids nutritional movements.

Espinosa saw under the influence of coca a notable increase in the excretion of urea and uric acid, as well as of phosphoric acid, and an increased exhalation of carbonic acid by the lungs. Of two rats starved by Moreno y Mais, the one that was given coca died in five days, having lost one-half more weight than the other which took no coca, and this rat survived. Demarle also concluded that emaciation was not prevented by coca, which therefore cannot be assimilated with caffeine and arsenic. These moderate the nutritional movement while cocaine accelerates it.

As with most plant remedies, cocaine does not exactly represent the effects of coca, and it is evident that there are other active agents in the leaves, in variable amounts and proportions. The yield of cocaine varies from 0.8 percent down to 0.2 percent; the other alkaloids being more plentiful when the cocaine is less. The extraction is difficult. Cocaine is made synthetically, the product being identical therapeutically with that from the leaves.

Liebreich says that cocaine acts on all the nervous centers beginning with the cerebrum and ending with the spinal cord. The stimulant effect is far more prominent from small doses. It is not a nerve poison but only "surfeits the cells with food." The greater the brain and the higher the temperature, the smaller the dose that will cause convulsions. It increases the quantity of air in the lungs by first increasing and then decreasing the rate of breathing. This indicates that in fever more effect may be seen from cocaine than in health.

Small doses do not affect the lumen of the blood-vessels; medium doses cause strong contraction, and large doses dilation from activity of the vasomotors. Applied to mucous membranes, cocaine solutions cause contraction of the blood-vessels with cylindrical epithelium sooner than those lined with the tesselated variety; and sooner with children than with adults. The cerebral vessels are rarely altered. The heart-action is uninfluenced by small doses, accelerated and even strengthened by medium doses and slowed by large ones. Cocaine cannot completely stop the heart.

There is a rise also in the venous pressure after medium doses of cocaine, and a fall after large ones. Small doses increase the working power of the muscles, more in those that have been at rest than in those that are already fatigued. When cocaine is taken during long marches the muscles recuperate very quickly on rest. But intermuscular injections diminish the force.

When administered by the stomach cocaine can manifest its effects in twenty minutes; by the subcutaneous method in ten minutes. It appears first in the urine. It is eliminated by the mucous membranes also. When convulsions and dyspnea appear albumin and sugar may be found in the urine. The urine is increased (Liebreich), but mucous secretions are lessened.

The use of cocaine as a local anesthetic dates from Koller's publication in 1884. The remedy must come in contact with the tissue to be anesthetized, when all varieties of sensation are dulled. Or it may be applied to the trunk of a nerve. On the unabraded skin it has no influence unless driven in by cataphoresis. The motor nerves are affected as well as those of general and special sense. The tip of the tongue cannot be anesthetized by the strongest solutions. Applied to the eye it contracts the vessels, causing a slight sense of burning, followed by dryness, coldness and pallor. The lids open wider, the pupils dilate, there is anesthesia and analgesia of the cornea and conjunctiva, but not of the iris.

These phenomena appear in one to three minutes and last five to fifteen. Intraocular pressure is first slightly increased and then lessened. Accommodation is slightly limited, but never paralyzed. Exophthalmia may be simulated. Mydriasis comes in ten to twenty minutes and lasts some hours, or a day. The dilation can always be increased by atropine. Solutions of one to two percent are strong enough for the eye.

Cushny attributes the rapid pulse to stimulation of the accelerator mechanism rather than to sedation of the inhibitory apparatus.

If so, cocaine is not a direct antagonist of aconitine. Constriction is due to direct stimulation of the vasoconstrictor centers for section of the splanchnics relaxes the vascular tension. Total anuria for hours sometimes follows the use of cocaine, so that it seems likely that the effect on the kidneys is due to its action on the blood-vessels. Cocaine may be termed a general protoplasmic poison.

Van Renterghem thus describes the results of his experiments in testing cocaine on his own person: Between noon and 4 p. m. he took ten doses of Merck's pure cocaine, each of ten centigrams, about 1.5 grains. The drug was allowed to dissolve in the mouth that the local effect could be studied at the same time. During the four hours he thus took 870 milligrams of cocaine, or about 14 grains. After the second half-hourly dose he felt no longer the slight tendency to sleep which had ensued after a bad night; after the third dose an agreeable sensation, like that of slight alcoholism. Cerebral activity ensued, he worked with pleasure, thoughts followed each other quickly, the judgment was more prompt; the humor was gay; he felt benevolence for all the world. This state was maintained throughout the experiment. After the seventh dose he perceived an agreeable warmth, his respiration normal. He felt a desire to talk without cessation and to be in movement. He felt the capacity to lift great weights. These symptoms lasted three hours after the last dose, then slowly subsided, so that by 11 p. m. everything had returned to the normal state. At noon the pulse was 74, temperature 37.4° C. in the armpit; when the last dose was taken the pulse was 110 to 120, temperature 37.4 in the anus, 37.9 under the arm; at 11, when retiring, temperature under the arm 37.4, pulse 76. During the evening, which was passed at the theater, he felt no exhaustion, no fatigue. Dining at 4:30 he felt no hunger but ate mechanically as was his custom. The loss of taste may have explained this. He would have been as well satisfied to miss the meal. Digestion was good; no effect on the stools or the urine. Retired at 11:30, after a light repast, and passed a good night. At the moment of retiring he felt his head a little contracted, slight indication of aching in the forehead, above the eyes and at the vertex. Next morning this was still present, and it lasted till noon.

Experimenting upon himself Von Schroff found small doses increased the activity of the brain, while large ones, after a brief period of excitation, depressed the activity of the brain and caused somnolence. Fronmueller observed vertigo, delirium, ringing of the ears, and slumber. Plass experienced vertigo and a sense of feebleness.

The vast majority of persons addicted to the cocaine habit acquire that accomplishment through the use of nostrums containing that drug, especially when used for hay fever and catarrh. Many morphine habitues add the use of cocaine, which enables them to use more morphine and prolong the waking period, that of euphoria. Physicians in busy practice also acquire the habit to enable them to work beyond their natural strength. In the South it is said that the negroes are becoming addicted to this dangerous drug; and it is now known that the frightful crimes for which lynching is applied are frequently due to cocaine.

The cocainist uses the drug almost constantly, injecting or snuffing a few drops of solution every few minutes. He is restless, constantly on the move, facile, an easy talker, good companion, tells good stories, but tends to ramble on disconnectedly. He sits up all hours of the night, writing endlessly, the product of the night's labor being found scattered over the floor in the morning. Ask why he uses cocaine and he cannot tell. The most remarkable symptom is his utter lack of the moral principle. Obligations sacred to even the most abandoned have no importance to him. He is cunning, devises most plausible schemes to obtain cocaine. Once succeeding, he makes no effort to keep up the deception, regarding it as a joke, and depending on his wits to devise another scheme when a new supply is needed. Later he suffers with hallucinations, gets to picking "cocaine bugs" from his skin, thinks he is pursued by mobs for wholesale murders he has committed, etc. He rarely stops with cocaine but seeks to add all other habit-drugs of which he learns the use. Thus one man used morphine, tobacco, cocaine, absinthe, whisky, menthol, chloroform, cannabis indica, and hyoscine.

After a pretty large experience with various drug habits, the writer is skeptical as to the curability of the cocaine habit when once fully formed. Nothing is needed except deprivation of the drug, as no special suffering ensues from its discontinuance. But the patient is utterly untrustworthy, and will secure the drug unless confined as in an insane asylum. Such restraint for a year is the only means of cure; and in one such case, after years of freedom the man went deliberately back to the drug and killed himself with it. Another, after six months in an asylum held himself straight for nearly two years, and one day killed himself with an overdose. One man has remained free for ten years and is to all indications cured. It is almost the only exception in the writer's knowledge; and this applies to persons treated by every real expert and secret nostrum dispenser in the country. One man has been to seventeen

sanitaria for drug habits, and is now practically a life inmate. The difficulty is the absence of the moral sense, and consequently of any real desire on the part of the habitue to be cured. In this there is a radical difference from the morphine victim, who in even the last stages revolts against his slavery and dies purposely if he cannot break his chains. The writer has never seen evidence of a restoration of the moral sense after it has once been extinguished by cocaine.

Another characteristic of the cocainist which should have been mentioned is his insensibility to pain on the one hand and his exaggerated way of talking about it on the other. He will use the dirtiest ditch water for his solutions, half fill his syringe with the dirty mixture and inject dirt, air and all into a vein to get quick effect, with the most absolute indifference to results. The writer has known men to do this purposely to demonstrate the harmlessness of injecting air into the veins. If abscess or ulcer results, so much the better, for this gives him an excuse for obtaining more cocaine! But inflict on him the most trifling suffering—even the prick of the hypodermic he has used hundreds of times, and he will complain for weeks of the "sufferings of the damned" caused by it.

Sollmann says: "On the first introduction of the leaves into Europe the effects were disappointing, and the statements of the explorers were regarded as travelers' tales. These disappointing results were due to the fact that the sensations for which it is employed by the natives—hunger and fatigue—did not exist in the experimenters." The queer thing about this is that Sollmann is a member of the famous Council of Chemists and Pharmacists, which condemned cactus on exactly that sort of experimentation—on healthy subjects.

Sollmann summarizes the action of cocaine: It is a strong protoplasmic poison, paralyzing all cells with which it comes in contact, acting more strongly on some than on others. Its local application paralyzes nerve cells, fibers and endings, sensory nerves being most sensitive. It causes local vasoconstriction. It dilates the pupil by direct or systemic administration, by sympathetic stimulation, central and peripheric. On systemic administration it causes irregular descending stimulation and paralysis of the entire central nervous system. It causes a specific rise of temperature by stimulating the thermogenetic center of the caudate nuclei. It causes a vacuolar degeneration of the liver cells in rabbits. Its continued use leads to a habit resembling morphinism. Cocaine is almost

completely destroyed in the body, not even ecgonine being found in the urine.

Synergists.—Caffeine like cocaine excites the cerebral cells and the muscular system. Strychnine increases the excitability of the spinal cord. Cicutine and brucine, as well as yohimbine, cause local anesthesia and analgesia. Atropine paralyzes the cardiac inhibitory nerves, and dilates the pupil. Aconitine also dilates the pupil, but in its general action is antagonized by cocaine even more exactly than by atropine.

Incompatibles.—Hydrochloric acid breaks cocaine up into ecgonine, alcohol and benzoic acid.

Therapeutics.—The local applications of cocaine are too well known to require enumeration. Solutions may be applied to the unbroken mucous membranes but the cutaneous epithelium bars its action. It is used subcutaneously along the lines of an operation, or injected at some part so as to come in contact with the trunk of the nerve at whose distribution anesthesia is desired. Injected into the spinal canal anesthesia of the entire lower extremity including the pelvic organs is induced. This has been utilized to secure painless parturition. One nice local application is in the removal of foreign bodies imbedded in the cornea. The cocaine not only anesthetizes the cornea but the contraction of the vessels often releases the foreign body and facilitates its removal. Cocaine is also applied locally to reduce reflex action and to relieve pain, such as neuralgia, where the salt is injected along the course of the affected nerve.

The hydrochlorate of cocaine is the salt used, and it is soluble in almost any proportion in water, alcohol, alkaline solutions, glycerin, oleic acid, etc. Solutions lose their value soon, and should be prepared freshly when needed.

Internally cocaine has been recommended as a means of tiding the morphine habitue over the withdrawal period. The writer has given it a full trial, and the invariable result of this medication has been that the suffering is simply postponed and recurs when the patient is less able to bear it; while the patient is too apt to add the cocaine habit to his preëxisting ones.

Wood recommends cocaine as a cardiac stimulant in pneumonia, alternating with strychnine, and claims that the effects of the latter are thus supplemented. But this author has apparently not tried the use of strychnine by cumulative dosage. There is nothing in the studies of the physiologic action of cocaine here recorded to indicate its use in this manner. Indeed, the well-known variability

of this drug as to its effects on individuals renders it improper for use with those on whom it has not been tried. For while large doses may be well borne by one man, another may be injuriously affected by even half a milligram—gr. 1-134.

Special care must be taken in administering cocaine to alcoholics, who are apt to react unfavorably to it. But in threatened mania-a-potu a combination of cocaine with capsicin has proved quite effective. Here gr. 1-12 to 1-8 of cocaine with the same dose of capsicin may be given every one to two hours. This has dissipated an impending delirium tremens that seemed unavoidable.

The untoward effects described are attributed by Liebreich to other active principles in the coca, not separated from the cocaine in the process of extraction. The use of synthetic cocaine or of eucaine is not liable to this uncertainty. The writer has witnessed alarming heart failure, syncope, etc., continuing and recurring for hours, after cocaine had been used locally or internally. A sense of debility, malaise and anxiety are common. There may be excess or failure of any of the secretions or functions of the body. These symptoms may end in collapse.

The treatment of cocaine poisoning consists in the evacuation of the stomach if the drug had been taken by that route, and the administration of stimulant doses of morphine—gr. 1-8—of ammonia, glonoin for syncope, and strychnine to sustain quickly the heart and respiration.

Van Renterghem recommends cocaine internally for vomiting due to gastric hyperesthesia and excited by the contact of food; and in gastralgia or gastric ulcer.

Rabuteau recommended cocaine in diabetes mellitus and in albuminuria, believing that its action enhances the combustion of saccharine and albuminoid matters, which are thus utilized instead of being eliminated as a loss. He also advised it for phthisis, to increase the digestive powers. Under its influence he saw the appetite increase and the vomiting cease, even with subjects in the third stage. But as cocaine increases waste, the arsenates, or caffeine, with the hypophosphites, should be also administered to retard the movement of assimilation and disassimilation.

When given to enable one to bear unavoidable fatigue or prolonged exertions and exposure, the action of cocaine is increased by adding strychnine and caffeine. But that this is a ready mode of establishing the cocaine habit scarcely needs to be said.

Manassein found cocaine effective in relieving the vomiting and collapse of cholera morbus. Shoemaker says it sometimes

relieves migraine promptly. For vomiting of pregnancy and for seasickness it is often useful. The dysphagia of laryngeal tuberculosis may be relieved by cocainizing the affected parts before meals. Thorington found it useful in yellow fever.

Bartholow praised it in hiccough, asthma, chorea, paralysis agitans, senile tremor and that of alcoholism. An Algerian physician reported that cocaine was markedly tolerated in smallpox and beneficial. Bauduy advised it in melancholia, but others deny its utility here.

Burggraeve found cocaine useful in dyspepsia, very useful in gastralgias and in vomiting due to gastric hyperesthesia, also in the obstinate vomiting of pregnancy. It has been employed with advantage in very painful and rebellious hemicranias; in which Laura associates it with caffeine, aconitine and gelseminine. Cocaine often ameliorates excessive hunger and very intense thirst, physiologic or pathologic. Laura praises it as of great efficacy in the morphine habit. Some have vaunted it in phthisis, as a sedative, a vital incitor, or a regulator of the metabolism so exaggerated during the febrile periods. Here Laura associates cocaine with iodoform, aconitine and codeine, with a success he acknowledges to be scarcely credible.

Burggraeve injected cocaine hypodermically into the upper inner part of his thigh, relieving urethral strangury "as if by enchantment." He praised it in surgery and as a means of relieving painful spasmodic conditions, without causing dryness of the throat like atropine. He found it promptly effective in stridulous affections, laryngitis, bronchitis, asthma, etc. To the list of maladies in which its antispasmodic powers render it available, Laura adds vaginismus. This accomplished clinical therapeutist also finds cocaine useful against gastric neuropathies, even rebellious hysteria, and spasmodic, idiopathic gastralgias and enteralgias. Vinaj and Tosi got remarkable progressive amelioration from it in a very grave case of hysteroepilepsy, with the characteristics of a hereditary neuropathy, in which metallotherapy, electrotherapy and hydropathy, employed with the greatest skill, had failed.

Among the numerous local applications that have been made of this potent anesthetic we mention those of Campana, to ease the pain of syphilitic and other skin diseases, before applying caustics; Cerasi, for painful and itching maladies; Obissier, for anal fissures; Andoni for cracks in the breast of nursing mothers; Peters for gonorrhea; Paget for acute coryza; Weiss for burns. The hemostatic effect is remarkable.

Bettelheim applied it to relieve vesical tenesmus. C. F. Taylor some years ago called attention to the valuable fact that when remedies like cocaine were applied to the mouth of a duct leading to any hollow organ, the effect was transmitted to that organ. Thus, to relieve vesical tenesmus the cocaine need only be applied beneath the prepuce, and the relief will be as great as if the remedy were injected into the bladder.

In nervous dyspepsias cocaine may be given alone or associated with caffeine and quassin; if there are pains or cramps adding codeine or hyoscyamine. Semtchenko strongly advised the frequent instillation of cocaine solutions in infantile coryza, believing that the serious danger of its spread might thereby be prevented. Labric first applied it locally in whooping-cough, and Groeffner extended its use to all nervous coughs. Laura urges its local application in asthma, spasm of the glottis, laryngismus, false croup, spasm of the esophagus or of the stomach, gastric ulcer and in bulimia. Courserant applied it locally for photophobia, blepharospasm, idiopathic ophthalmia, ulcerative keratitis and simple iritis. Keyser, however, called attention to a case of panophthalmitis following its local application to the eye. Cocaine salts are insoluble and inert in fats or oils, excepting the oleate of cocaine. Schneider injected cocaine salicylate hypodermically for trigeminal neuralgia, "with surprising success." Bergiotti had a similar experience with it in hemicrania and spasmodic strangury.

For internal use Laura advises the granules containing each 1-134 grain of cocaine hydrochlorate. Of these he advises for adults one or two, for children one frequently repeated until the effects are manifest. Wood gave 1-8 grain between four-hour doses of strychnine as a stimulant in low fevers.

The alarming symptoms of collapse occasionally following the local use of cocaine are, it is claimed, only liable to follow the use of solutions whose strength exceeds 2 percent.

One of the most valued applications of cocaine is to relieve the intolerable suffering of laryngeal tubercular ulceration, and allow the patient to swallow food in comfort. In ulcer of the stomach, also, great relief usually follows a dose of 1-8 grain in solution, and this is more effective than morphine.

The hemostatic power of cocaine is remarkable, especially since it is promptly manifested in the capillary hemorrhages, purpura, hemophilia, etc., where the ordinary hemostatics are ineffective.

Taken altogether, considering the remarkable properties of this alkaloid, surprisingly little is to said as to its internal thera-

peutics. This is largely due to the danger of the habit, which renders it even more perilous than morphine, as the formation of the habit of cocaine is so much more insidious. There are thousands of cocainists who have not yet found it out. The writer has tried the use of coca in training boat crews for races and found the same crew did better without it. Whatever it does when the fresh leaves are chewed in Peru, no such effects as are described are obtainable from cocaine or from any of the preparations, officinal or proprietary, to be found in the shops. Possibly, as Rusby suggests, there is a volatile element in the fresh leaves that is lost in drying them.

These considerations greatly contract the therapeutic field, as cocaine is too dangerous a drug for general use. Whenever the physician sees fit to employ it he should take the utmost pains to keep the knowledge of it from his patient, and never allow the latter to have a prescription that would enable him to obtain the drug again without the consent of his medical adviser.

Better be certain, and don't prescribe it at all; but if you *must* employ it, dispense, in a well-disguised form.

The dose of cocaine internally for any sort of vomiting is gr. 1-67 every fifteen minutes till effect. As a cardiac stimulant in pneumonia gr. 1-6 may be given every eight hours with a dose of strychnine alternated. Many of the effects attributed to coca, therapeutic as well as toxic, are undoubtedly suggestive.

Since brucine is a local anesthetic and a heart tonic as well, the writer has employed a two-percent solution of the hydrochlorate with two percent of cocaine added, in those cases where the use of cocaine alone was followed by symptoms of syncope or collapse. This has proved successful in every case as yet tested with it.

CODEINE

Standard granules—gr. 1-67, Gm. .001; gr. 1-6, Gm. .01.

Formula—$C_{17}H_{18}(CH_3)NO_3 + H_2O$.

Codeine was discovered in 1832 by Robiquet. Chemically it is a methyl morphine. It is soluble in alcohol, ether, chloroform, benzole, petrolether, amylic alcohol and diluted acids, fairly soluble in water and slightly in ammonia. It is a strong base, and a number of salts are listed. The phosphate is especially soluble in water. Van Renterghem takes occasion to say: "Chemistry, which has isolated the different principles of opium, and experimental physiology, have taught us their modes of action; so that it is quite natural for the clinician to reject this dangerous composition, this

double-edged tool, as Hufeland termed it, and use only the principal extractives, of which one can always measure the action."

Binz says: "In prescribing opium, the physician gives to the patient a complex substance which can produce inconvenient and uncontrollable effects since they depend on the richness of the medicament, always variable, in diverse active principles. In grave cases where he desires the narcotic action—that of morphine—he should avoid prescribing opium."

Water at 60°F., dissolves pure codeine 12.6 parts in 1000; at 212° F. it dissolves 58.8 parts. Crude opium yields about 0.6 percent of codeine. Codeine has been prepared synthetically by heating an alcoholic solution of morphine with soda and methyl iodide.

Physiological Action.—Van Renterghem one evening took 100 milligrams of codeine in divided doses. There resulted slight redness of the face, slight excitement of the nervous system, but sleep did not supervene till late. The sleep was light, troubled by dreams; on waking he experienced pressure at the temples, disagreeable sensation in the head, and absence of appetite. Though the usual dose of saline was not taken there were liquid stools. At 1 p. m. next day, after a good walk in the open air, all signs of the intoxication had vanished.

The same observer has often taken at bedtime a single dose of codeine, 10 milligrams, with sleep following shortly. This sleep was profound, and the waking was without discomfort, but he felt a sense of well being and restfulness.

Rabuteau found doses of 150 milligrams produce within half an hour muscular fatigue, with itching especially in the extremities, and pupillary contraction, lasting more than a day; there was no sleep, scarcely the beginning of somnolence.

Bardet found no effect from doses under three grains, which caused heaviness of the head, muscular weakness, but no hypnosis. Six grains caused such weakness that walking was impossible; often with pruritus and twice with erythema.

Huesemann found codeine in small doses hypnotic, but in large doses the effect approximated that of picrotoxin.

Van Renterghem resumes the evidence and concludes that codeine in small doses has an action calmant, lightly hypnotic, quieting the sense of hunger, neither constipating nor deranging digestion; in large doses it excites, causes agitation, headache, inappetence, nausea, vomiting and may lead to convulsions. Experiments on animals seem to show a more pronounced convulsant

action than that of morphine. Liebreich found from codeine an increase of reflex excitability of the spinal cord, going with increased doses to tetanic convulsions, and death from asphyxia and general paralysis. He notes from large doses also a sense of heat, trembling of the muscles and slowing of the pulse.

Cushny says codeine depresses the brain less than morphine and stimulates the cord and medulla more. The respiration is not so much slowed and may even be accelerated.

Barney, comparing morphine, codeine and narceine, insists that the convulsive element in opium appertains more to codeine than to morphine, and still more so than to narceine. The same authority says that while codeine is an innocent remedy in small doses, it should be better known that there is a latent convulsive power in it which may steadily develop when the dose is too high. This shows itself surprisingly in experiments with codeine on young animals, even in small doses. The constant lowering of temperature by codeine is well ascertained. Codeine blunts sensibility far less than morphine and does not make the nerves so sluggish as the latter. The awakening is much more healthful and natural from codeine than from morphine.

Robert Tissot says that the toxicity of codeine is one-tenth that of morphine. Codeine easily produces convulsions, especially in infants, and the convulsions occur suddenly without warning. It abates the excitability of the respiratory centers, lessening the number and amplitude of respirations, with a diminution of the quantity of air expired. He prefers it to heroine. In the small cumulative dosage it never causes accident. He approvingly quotes Dornblueth as employing codeine for neurasthenia.

Tauber states that codeine is mainly excreted by the kidneys.

Murrell items codeine as merely a little morphine, acting similarly in larger doses; but this is not borne out by the foregoing account.

Therapeutics.—As a hypnotic and antispasmodic codeine does not replace morphine, but may be used where it does not agree. Cushny also prefers codeine for the insomnia of melancholia. When there is any tendency to cerebral hyperemia codeine is preferable to morphine. While either will induce a drug habit codeine is somewhat less liable to do so.

Brunton and Freund claim that codeine has a specific effect in relieving pains of the intestines and ovaries. It has also been advocated for blepharospasm, photophobia, sciatica, gastralgia, bulimia, hepatic and ovarian colics.

But it is in affections of the respiratory apparatus that codeine finds its chief use. It soothes the disposition to cough and promotes freer expectoration. Van Renterghem combines codeine with iodoform, to calm coughs, and soothe pain in the alimentary canal. In dry coughs he gives codeine with apomorphine, especially in late phthisis. With cicutine or helenine it is serviceable in spasmodic coughs. Given with veratrine it prevents irritation of the stomach in those who cannot take the latter alone. In gastralgia, enteralgia and pains about the neck of the bladder, codeine acts as an anodyne without interfering with the digestion or constipating. Here he associates hyoscyamine, atropine, cicutine and the vital incitant, strychnine. In infantile practice codeine replaces morphine generally as an anodyne and hypnotic; also in women, aged persons and those menaced with congestions of the brain (Gubler).

Trousseau also recommended codeine in acute bronchitis with hyperesthesia and spasm of the bronchi, and constant cough.

Vigla and Aran recommended codeine in bronchorrhea and intestinal relaxation, to lessen mucous hypersecretion.

Codeine has been extensively employed in the treatment of diabetes mellitus and insipidus. It lessens the excretion of urine and the output of sugar. The doses here have been raised to 15 grains a day, there being a special tolerance of the drug. It is doubtful if codeine possesses any special advantage here over morphine except for the absence of ill effects in the alimentary canal. Shoemaker says some cases are cured and many benefited by codeine. Van Renterghem speaks well of this agent in strangury, in chronic urinary affections. He recommends here codeine with atropine and cicutine.

Lochbuehler thinks codeine has a special control over serous inflammations. Brunton credits it with a specific influence over the sympathetic, and recommends it for the severe pains of perityphlitis, abdominal tumor, fecal impaction, cancer of the liver and pancreas, and appendicitis.

Dornblueth preferred codeine to hyoscine in sedating the insane, when the latter caused hallucinations, and if there were anxiety, precordial distress or insomnia.

Sollmann says codeine shows a slighter quieting and a stronger excitant action than morphine. With the former the maximum of hypnosis is soon reached, and on further dose given the depression ends and excitement supervenes. Codeine approaches heroine in its predilection for acting on the respiration, depressing the sensitiveness of the center and the reflex irritability that arouses cough-

ing. The volume of individual respirations is increased. It may increase the consumption of oxygen. It stimulates the spinal cord, increasing reflex irritability, and may in large doses induce convulsions. Locally applied it temporarily destroys the activity of the nerve ganglia and fibers. It increases the excretion of carbonic acid. About 80 percent is excreted unchanged, mainly by the kidneys, some in the feces.

Bouma asserts that the continued use of codeine does not lead to its increased destruction in the body nor to tolerance. The latter is certainly a mistake.

Robiquet observed that doses of 20 to 30 milligrams caused a sense of well-being and calm, with tranquil slumber and a refreshing awaking. Bardet advised doses of 20 to 80 centigrams, but Laura found that such huge doses were followed by the symptoms usual after overdoses of morphine. Cantani pronounced it a fine hypnotic, and Laura insists that this property inheres only in little doses. Burggraeve says codeine is an excellent calmant for the nervous system, especially for peripheric irritations, and it does not tie up the system like morphine. Codeine neither causes nor maintains constipation. He employs codeine instead of morphine for young infants, for persons of exaggerated sensibility, and for those who for any reason do not tolerate morphine well. Budberg employed codeine for the cerebral irritations induced by tobacco, for violent odontalgias, and for hepatic colics, with decided success. Laura prefers it as a hypnotic when the insomnia is due to an irritation, to nervousness, or to nervous inquietude; he uses it for spasmodic coughs, in the middle period of whooping-cough, as an auxiliary to calcium sulphide; in the nervous cough of dentition; in that obstinate cough of phthisis, worse in the evening and at night, with which little doses do better than big ones—a few milligrams given in quick succession. Sometimes camphor monobromide, hyoscyamine and aconitine, according to the grouping of symptoms, may be associated with excellent results in mild catarrhs and in the bronchites of the tuberculous. A long experience enables him to fearlessly administer codeine for intestinal irritability with diarrhea.

Barbier declared that codeine could be given continuously without forming a habit, but this is a mistake. Magendie found that one grain of codeine produced calm and restful sleep, not followed on wakening by somnolence and head-heaviness. Two granules excited nausea and vomiting. One granule, Gm. 0.001, dissolved on the tongue, often relieves cough.

Solon tried codeine in phthisis, finding that two grains in twenty-four hours lessened the cough, stopped paroxysmal attacks and gave the patient peaceful sleep.

Krebel succeeded with codeine in nervous insomnia. Berthe secured rest from it in a case of gastralgia, where every other remedy had failed. Szerbeki used codeine successfully in abdominal neuroses, notably in the celiac variety. Much of the difficulty experienced in using codeine is attributed to impurities in the commercial salt.

Dornblueth advised codeine in ascending doses in the treatment of neurasthenia, especially that form due to intellectual overwork with incessant somnolence.

Polack, investigating codeine, came to these conclusions: It is not an indifferent remedy, intoxication may follow one-grain doses, it is a useful narcotic, but nothing else, it is not curative of any disease, it should not be recommended in any painful affection with few exceptions, it does not produce a definite action on psychic affections and on the nervous system; in the alcohol, morphine and arsenic habits during the period of withdrawal it is of no use, and there is danger of establishing a codeine habit; it is useless in inflammations of the genital organs, but may be useful to continue the calm once secured from morphine; it acts well in affections of the respiratory passages, and in some of those of the intestinal tract and urinary passages.

Merck's codeine is about half the strength of morphine. The dose for an adult, single, at bedtime is gr. 1-6; for an infant from 1-134 to 1-67. Either may be repeated every half-hour if needed. The same care should be exercised as in administering morphine.

COLCHICINE

Standard granule—gr. 1-134, Gm. .0005.

Colchicine is the active principle of Colchicum autumnale, meadow saffron, and is found also in other species of colchicum. It is doubtful if colchicine ranks with the alkaloids, as a pyridine derivative, since it has an acid reaction. It is soluble in water, alcohol, ether and chloroform. Formula: $C_{22}H_{25}NO_6$ (Merck); $(CH_3O)_3C_{15}H_9(NH.C_2H_3O).CO_2.CH_3$ (Beilstein).

Colchicum has fallen into disuse through the uncertainty of its preparations.

Zeissl obtained colchicine by treating the seed with 90 percent alcohol; the alcohol is then removed and the residue dissolved in

distilled water, and shaken up with chloroform absolutely free from hydrochloric acid. When the chloroform is distilled off there remains a syrupy residue, which on rapid cooling, deposits rosette crystal-groups. This is purified by adding small quantities of pure chloroform; the colchicine is taken up in a large quantity of the same solvent, condensed, mixed with ether, and crystallized from this. The result is a combination of colchicine with two molecules of chloroform, the formula being $C_{22}H_{25}NO_6{}_2CHCl_3$. On evaporation chloroform is given off, but not all of it, even on prolonged heating. The crystals are luminous in the dark. When free from chloroform, colchicine is amorphous, bright yellow, darkening on exposure to light, with strong electric qualities when triturated. Zeissl's colchicine is lævogyrous. The addition of mineral acids, or boiling with alkalies, splits off a methoxyl group, leaving colchiceine, or aceto-trimethyl-colchicinic acid.

On heating colchicine with hydrochloric acid to 302° F., ammonia is split off. Colchicine gives no salt with acids, and is not precipitated with platinum chloride. Concentrated nitric acid dissolves it, giving first a violet, then a yellow color. Sulphuric acid containing nitric acid gives at first a yellow-green, passing over gradually to green, blue, wine-red, then again yellow, and on addition of concentrated caustic soda solution, it becomes red. Bromine water gives a yellowish precipitate, and potassium iodide a brown. Boiled in iron chloride it colors this acid solution green to dark green, and shaken up with chloroform this becomes brownish to red. Mercuric chloride produces in the hydrochloric solution a lemon-yellow precipitate, as do gold chloride, cadmium iodide, potassio-mercuric-iodide, potassium bismuth iodide (yellow to brown), phosphor-wolframic and phosphor-molybdenic acids. Potassium chromate and sulphuric acid give a dirty orange-yellow precipitate. Tannic acid gives a white precipitate. Picric acid gives no precipitate. Solution of phenol gives a milky coloring, which after some time condenses into resinous little drops.

Colchiceine gives salts with bases and acids, and with gold chloride a double salt. In the same way colchicinic acid, dimethyl and trimethyl colchicinic acids combine with acids and bases (Liebreich).

The physical and chemical properties of colchicine were not well known until after the labors of Houdé.

Crystallized colchicine, as obtained by Houdé's process, appears in the form of long needles, sometimes colored, but obtainable pure and uncolored by redistillation in chloroform and then in

petroleum-ether. By this process he gets from one kilogram of colchicum seeds 3.35 Grams of crystallized colchicine, while from the bulbs we get no more than 0.45 Gram. All parts of the plant contain some variable proportion of colchicine until we come to the anthers and pollen, which give only traces of it.

Colchicine has an agreeable odor, a very bitter taste, without burning but persistent. It is very soluble in 90-percent alcohol. It is levogyrous in polarized light. Its action on litmus is almost imperceptible. It is therefore properly said to be not an alkaloid but rather a nitrogenized body.

Colchicine acts on the nervous system of the secretory organs and on the glandular apparatus, both great and small. This action shows itself in the kidneys, in the liver and in the small intestines by phenomena of irritation, exaggerating the functions of these organs, an exaggeration which results in a considerable effort to eliminate from the organism those elements whose habitual presence in the economy is characteristic of an arthritic disposition or diathesis and an excess of which constitutes the arthritism which we know as gout.

Colchicine also produces irritating phenomena in the articulations and in the marrow of the bones. Anatomopathologic researches have shown that after using colchicine experimentally noticeable quantities of the drug were found in the osseous and articular tissues and in the muscles near the articulations. Colchicine therefore carries on its action electively against those regions for which gout has a marked predilection, and it is by an irritant action that this active principle produces its therapeutic effects. Before the experiments mentioned were made it was noticed that there was a certain unaccountable feeling of dulness around the articulations after colchicine was administered. This is now explained.

The irritant action of colchicine shows itself on the intestines by serous diarrhea; on the liver by an increase of bile; on the kidneys by a more abundant diuresis and at the same time a greater proportion of uric acid in the urine thus increased and also in the serous diarrhea caused by colchicine.

On the part of articulations the phenomena of irritation which colchicine produces result, thanks to its action on the vasomotors, in a considerable removal of uric-acid deposits from the articulations toward the emunctories whose function it is to carry these deposits out of the organism.

Everything, therefore, in the action of colchicine contributes to the desired result, to-wit, drainage of the economy to rid it of the noxious abnormal accumulations and its retention in the blood,

where it would produce crises of gout and of gouty states. It is no wonder, therefore, that by whomsoever the physiologic mechanism of colchicine was studied, this alkaloid should be considered as a specific against gout.

According to Mairet and Combemale colchicine increases the excretion of uric acid. It produces congestion in the articular surfaces and in bone-marrow, giving place to two interesting effects which come near those of purgation and thus explain the mechanism of the action in arthritic diseases generally and in gout specially: (1) it diminishes the uric acid of the blood; (2) it produces a substitutive action. That which goes on upon the articulating surfaces in gout goes on equally in all other organs that are the seat of arthritic manifestations. Many observations confirm the good reason for this opinion, and these observations increase daily, as physicians decide to employ this powerful remedy more frequently.

The great and capital indication for colchicine is arthritism in all of its manifestations. Acute or chronic gout, articular or visceral; acute or chronic rheumatism, gouty or deforming; gravel, obesity, gouty or rheumatismal neuralgia, in a word, all the multiple forms of rheumatism, are amenable to colchicine.

The arthritic diathesis is its favorite field of operation. But to understand well the mechanism of its action it is necessary to devote some lines to the history of uric acid in the tissues.

Modern discoveries have thrown some discredit on this doctrine of diathesis, and yet, as Sir Dyce Duckworth said in his remarkable lecture before the Faculty of Medicine of Paris: "The study of all modern discoveries must not make us forget the past, and our duty is to add the new to the old, and we must distrust that which is simply novelty and nothing more." This celebrated English physician reminded us in that lecture of the necessity of keeping in mind the four types of diatheses: The arthritic, the scrofulous, the nervous, and the bilious.

It is not our desire to enter here upon an examination or criticism of this classification. And yet, perfectly legitimate as Sir Dyce Duckworth's protest against forgetting the study of territory and the personal factor of disease is, still the current opinion outside this school, especially among experienced practicians, the notion of arthritic diathesis, i. e., the morbid state which manifests itself in pathologic alternations of gout, gravel, renal lithiasis, migraine, asthma, etc., was kept inviolable and intact.

A good number of ailments seem to arise in this arthritic diathesis from a particular state of humors in which uric acid plays

a primordial part. This state has often been designated by the term "uric-acid diathesis."

Let us take gout as an actual instance, which is a typical manifestation of this diathesis. Physicians and biologists agree as to the primordial part which uric acid plays in the pathology of these ailments, and however strong the efforts to lower the importance of uric acid as a factor in this disease, we are bound to adhere to the uric-acid theory, and so much the more since the therapeutic deductions drawn from this pathogenesis seem to confirm it.

The origin of uric acid, the causes of its accumulation in the blood and in the tissues enable us to understand how to fight against this diathesis.

Uric acid is one of Fischer's compounds of a group of purins, and the xanthin and the nuclein bases constitute the rest of the group. It is derived, according to Horbaczewski and other authors, if not altogether at least in great part from the nuclein and is therefore a product of nuclear disintegration. This nuclein comes in part from elements ingested (exogenous nuclein) and in part from the tissues of the body. According to Bence Jones and Roberts, uric acid is found in the blood in the form of a quadriurate composed of uric acid and urate. It is eliminated by the urine in proportion of 40 centigrams to one Gram per day (Osler), on an average of 70 centigrams (Hammarsten).

It is very sparingly soluble. It takes for one part of uric acid 1400 parts hot water, or 1800 parts of cold water to dissolve it. It cannot dissolve in the urine except by the formation of tribasic phosphates, which give place to the form of more soluble urates by ceding to the uric acid one equivalent of the base.

How comes about the accumulation of the uric acid in the blood? It may be by an insufficient diminution of the uric acid by way of the kidneys, they being insufficiently acting (Garrod's and Ebstein's theory). We may also think of a too slow destruction of uric acid by a retarded nutrition (Bouchard's theory). The organic combustions are not done completely, and the aliments introduced instead of becoming transformed into urea do not come further than to a transformation into uric acid only. The destruction may also be rendered insufficient in consequence of a primitive neurosis (Lancereaux's theory). This is equally the theory of Culler. Or there may be an exaggerated augmentation of the exchanges (Lecorche) or a nutritive deviation in the liver (Murchison's hepatic theory). Lastly, the accumulation of uric acid may be due to lack of solubility, the cause of which is (according to its authors) variable;

according to Schmoll it is the insufficiency of thymic acid. Uric acid will circulate in the blood by forming a different organic combination in the cells of persons in good health.

It was thought also that this default of solubility was due to a diminished alkalinity of the blood (Garrod, Haig,) but the labors of Magnus Levy have not shown this diminution of alkalinity to be constant.

According to Sir William Roberts the accumulated uric acid in the state of a soluble quadriurate in a medium rich in sodium carbonate fixes one atom of the base and becomes changed into insoluble biurate which deposits itself in the tissues.

We will not pursue further the causes of the uric-acid diathesis. We are now furnished with sufficient facts to understand that a good treatment of the uric-acid diathesis must needs modify the elimination of the urate of sodium and must modify the quality of the altered blood in order to abate the production of uric acid in excess, and this is just exactly what colchicine does. The best proof we can give of the efficacy of this substance in this great class of diseases is that colchicum has always been the base and frequently the only active medicament, avowed or concealed, of the innumerable remedies, secret or otherwise, which have been really efficacious against gout, beginning with the famous *hermodactylus* of the Greeks and coming down to the more recent specialties launched against this disease.

M. Lecorche considers the active principle of colchicum as the specific against gout, even superior to salicylate of sodium, which he does not think to be contraindicated.

The point must not be forgotten, moreover, Lecorche insists upon, that the many diverse manifestations of this pathologic condition will remain rebellious to all other tentative therapeutic measures so long as this medicament has not been administered; and to this it will sometimes yield with marvelous rapidity.

The most rational mode is the one-milligram granule of crystallized colchicine, whose activity is always the same and whose purity in the crystalline form is perfect. In this form only the physician will always obtain good results and never be disappointed.

Colchicine presents no other contraindications than diseases of the stomach or of the intestines, because of its easily irritant action on these organs when in a diseased state.

In the acute stage we give, where it is indicated, four granules the first day, three the second day, two the third day and one the following day. If needed we begin again in the same order.

In chronic cases we give two or three granules *pro die* for a longer or shorter period according to the results obtained.

As a preventive we give one, then two, three and lastly four granules, gradually increasing until we get to the limit of easy tolerance, then we go back one granule and continue to reduce the dose for a longer or shorter time according to the condition of the patient and his tolerance of the remedy.

In every case where one has to combat the arthritic diathesis in all its forms we administer the colchicine in the manner last mentioned.

Physiologic Action.—Two to six hours elapse after the administration of colchicine before its effects are manifest. Given by the stomach or subcutaneously in toxic doses gastric and intestinal discomfort are felt, then gastric pain, salivation, nausea, vomiting and diarrhea. The dejecta become mucous and blood-streaked, the vomit becomes bloody, the skin is covered with cold sweat. Depression, apathy and collapse follow; motion becomes difficult, especially in the legs, the motor paralysis becoming complete and creeping up until it reaches the respiratory centers, causing death by asphyxia. Muscular pains may replace the spasms (Wood). Reflex action is depressed (Albers). Vertigo and anxiety are usual, and sometimes confusion or delirium precedes collapse, but usually the mind is clear till death. The largest doses finally paralyze vagus-inhibition (Brunton).

The pulse becomes small and rapid in collapse, but there is no direct action on the circulation.

Respiration is at first deep and full, becoming shallow, death being due to paralysis of this center. The heart beats after death. The bowel-action is hurried by increased irritability of the nervous mechanism (Jacobj); and the mucosa is also irritated (Cushny). The muscles are affected as by veratrine, becoming quickly fatigued. Locally applied colchicine is intensely irritant. Cushny attributes the nervous symptoms to the collapse produced by the gastrointestinal irritation, with no direct cerebral depression. So also the collapse is attended by a consequent sensory paralysis.

Small doses increase the urinary fluid, the urea and uric acid excreted, but larger ones lessen or stop the fluid secretions (Paton). Hematuria occurs in animals. The symptoms are attributed by Cushny to the excretion of the colchicine by the bowels and the kidneys, and consequent irritation of these structures. Excretion may be concentrated upon either. Brunton places colchicine among the most powerful hepatic stimulants; in large doses also

stimulating intestinal secretion and peristalsis. He ranks it also as an alterative, improving nutrition in an unknown manner; and as a hydragogue diuretic. The effects are more marked on carnivora than on herbivora.

In man colchicum rarely causes more damage then a duodenal catarrh. In animals poisoned by this drug the post mortem shows evidences of acute gastroenteritis, ecchymoses, free blood in the alimentary canal, the blood being dark and coagulating with difficulty.

Brunton says that in continued non-toxic doses it causes anorexia, faucial irritation, flatulence, loaded tongue, uneasiness and pain in stomach and bowels, nausea and diarrhea, slow pulse and muscular debility.

Mairet and Combemale state that in doses of Gram 0.0002 to 0.0003, colchicine causes in healthy men mild headache, muscular weakness, abdominal pains, rapid pulse, thirst and diuresis; in doses of Gram 0.005, diarrhea and oliguria.

Van Renterghem took Gram 0.0005 of colchicine, every half-hour for 20 doses. Slightly increased peristalsis alone occurred. An arthritic patient took the same dose every hour for five days, in which he took Gram 0.035 in all, occasioning dyspeptic symptoms, not severe, subsiding on discontinuing the medicament. Colchicine administered hypodermically does not manifest its action for an hour. In its slowness of getting to work it contrasts with the promptness of veratrine.

Veratrine, aconitine, emetine and digitalin are in certain conditions synergistic to colchicine. Morphine neutralizes some of the effects, but favors the absorption of colchicine by soothing mucous irritability.

Colchicine is contraindicated by gastric or intestinal irritability, and when its use is followed by over-action, by pains, colics, etc. It should be contraindicated in phthisis, judging by its action, but observations on this point are wanting.

Most of the experiments made with colchicine are valueless, because the experimenters failed to observe sufficiently the variations of diet, by which the elimination of urea and uric acid would be influenced. Besides, under the name of colchicine a number of mixtures were employed, containing colchiceine, chloroform, and numerous by-products. Paschkis employed a pure colchicine, and his results, confirmed in the main by Rossbach, are therefore to be accorded more respect than others. Paschkis could detect no increase of blood-pressure from colchicine, but in cases showing

abnormally high pressure the drug occasioned a diminution. Sensibility was also reduced.

The conflicting testimony in regard to colchicine may be summed up in the statement that small doses increase the excretion of urine, as far as relates to the water, the urea and the uric acid; while large medicinal doses cause vomiting and diarrhea, due to the excretion of the drug through the mucous membrane of the stomach and bowels. As colchicine acts far more vigorously on carnivora, it is probable that it is more effective in those who eat too much nitrogenous food. Does colchicine increase the internal secretion of the kidneys or of the other organs? It is not found in the bile; but Shaller states that bile is always present in the evacuations produced by colchicine, and as it relieves hepatic congestion it evidently increases the activity of the liver. But as hepatic torpor is often associated with uricacidemia, the relief may be secondary to the general benefit of the increased excretion. And yet as urea is a product of the liver, does colchicine increase the production or simply the excretion of the bile? These queries, unanswerable at present, show how superficial has been the study of even the most popular articles in our materia medica.

Shaller says that colchicine increases the secretions of the liver, intestines, kidneys and skin.

Sollmann says the slowness of colchicine to act is due to the fact that it must be first changed to oxy-di-colchicine, formed from it in the mammalian circulation. Its action on the sensory nerve-endings and the heart is similar to that of aconitine and veratrine. To the central nervous system it is depressant, partly through the effect on the abdominal organs. It is one of the deadliest of poisons, as its effects once begun are not to be controlled.

Laura says that even in small doses colchicum causes lively irritation and even inflammation of the stomach, but it is not so with colchicine, of which he has given 15 to 20 granules a day without inducing vomiting, colics or considerable diarrhea, or any other of the phenomena that readily follow the administration of the crude drug.

Ruthendorf proved that colchicine increases both the formation and the excretion of bile. Garrod found that small doses rapidly developed the diuretic action, while Ruatta determined that large doses of colchicum exerted a contrary influence.

Burggraeve ranged colchicine with digitalin as a diuretic, finding the former useful in acute rheumatism and gout, but not in atonic forms of the latter. It should not be given at the beginning

of the paroxysm, but near its close, always in small doses, stopped at the slightest nausea. Diuresis and bilious evacuations are evidences of benefit. It is particularly useful in hypersthenic gout, in the young and robust; rarely permissible in the recurrent gout of the aged. Burggraeve combined strychnine arsenate and digitalin with it in gout. In substituting colchicine for colchicum we avoid the dangers, and escape the pains, many times atrocious and frightful; by associating aconitine the fever is moderated and ceases after a little while; and diuresis follows, which is always beneficent. The association with digitalin never fails to induce diuresis, and facilitates the excretion of urea or of uric acid. The addition of podophyllin or of saline laxatives provokes a more abundant biliary excretion and an intestinal flux without colic, the blood becomes *oily*, the organic exchanges are facilitated, and the red blood corpuscles are more avid for oxygen (Laura).

While Laura mentions the use of colchicine in acute rheumatism he gives preference to aconitine and sodium salicylate, sometimes adding scillitine. He gives a list of affections often associated with uric acid, in which colchicine may be employed—asthma, bronchitis, chronic urticaria, gouty dyspepsia, the cerebral symptoms of plethorics, and hepatic engorgements with lessened biliary excretion. This alkaloid has been recommended in gonorrhea, where antimony was once employed as an antiphlogistic to moderate the acute symptoms. In anemics it is necessary to guard colchicine with caffeine, atropine, or digitalin. Tonsut cured an epilepsy of eight years' standing with colchicine.

Therapeutics.—In gout colchicine has won the reputation of a specific, and especially in the acuter manifestations of this affection. The usual method was to administer enough of the drug to produce decided action on the stomach or bowels; and with this the acute pain and other evidences of the attack subsided. Whether colchicum is effective against the chronic forms of gout is not so clear, since victims of this malady, if relieved of the pains, are apt to indulge in the pleasures of the table to a still greater extent. But when the proper balance between the diet and the exercise is maintained, colchicine will prove of great assistance in eliminating from the body its excess of uric acid.

In America gout is represented by uricacidemia, and in the multifarious manifestations of this diathesis, colchicine is the first of remedies. It is not necessary to push the drug to the production of unpleasant effects. Let the granules be taken until slight looseness of the bowels is evident and then suspend the medication until

the next day. The daily dose thus ascertained, may be divided into three and taken before meals in the usual way.

Colchicine is more rapidly absorbed than the galenic preparations of colchicum, but the slowness of its action renders this agent ill fitted for rapid cumulative administration; so that the doses should be at least four hours apart. So numerous are the manifestations of uricacidemia, such as myalgic pains, headaches, catarrhs acute and chronic, itching and other irritations of the skin, gastrointestinal catarrhs with the numerous train of ailments pertaining thereto, that one cannot go far wrong in prescribing colchicine for a plethoric person or a carnivorous individual, sedentary by habit, who is complaining of these or of any anomalous ailment. And in this land, where most persons eat meat twenty-one times a week, there is perhaps no agent more generally useful. Give half a milligram or more at bedtime.

The great objection to colchicine is its remarkable efficiency. The melancholy, dullness, sluggishness, anorexia, bad breath, "tired feeling," are so promptly dissipated by a few granules of colchicine, that the patient, perhaps unconsciously, increases his consumption of meat and relaxes his exercise, relying on the daily dose of colchicine to keep him comfortable. It would be far better to forego the aid of all drugs, and let nature punish the slothful glutton until he is driven back to hygienic living.

Abbott reports excellent results in pleurisy occurring in rheumatics, from colchicine combined with aconitine and bryonin.

In gout, colchicine acts best with or following purgatives. In rheumatic gout, colchicine and iodides give relief (Brunton.)

Butler advises colchicine in full doses for ascites from hepatic obstruction, and mentions its use in gonorrhea, chordee, hypochondria with renal insufficiency, ocular inflammations, and local manifestations of gout. Abadie found colchicine, Gram 0.001 two to four times daily, of value in scleritis. Woodbury injects it into the nerve-sheath in sciatica, but Butler condemns this on account of the severe local irritation.

Merck gives the dose of his colchicine as Gram 0.005 to 0.0022, two or three times a day. I have rarely found it advisable to give more than Gram 0.0005 four times a day, and this will be too much for persons with delicate stomachs. In acute gout, or the cerebral congestions of plethoric persons, where a strong and speedy effect is required, give Gram 0.001, dissolved in hot water and repeated in two hours. Gelseminine, veratrine or lobelin may be added in cases requiring speedy relaxation.

In acute gout and rheumatism, Shaller advises Gram 0.0005 to 0.001, every hour, or oftener in robust cases, with aconitine, until the pain and fever are subdued, or the bowels thoroughly moved. After full action the doses should be reduced and the benzoates added. Delicate patients should take the drug less frequently. In chronic rheumatism with stiffness of the joints bryonin is a useful adjuvant. He reports two cases of obstinate sciatica cured by colchicine Gram 0.001 every two hours till free purgation, then Gram 0.0005 every three hours. In rheumatic neuralgia, quinine arsenate, Gram 0.01, should be added to each dose.

Treatment of colchicine poisoning: Empty the stomach and bowels if not already done, giving abundance of warm water. Tannic acid is the only known chemical antidote; it is not reliable but give it freely. Check vomiting and purging by morphine. Allay irritation by white of egg in water. Treat symptoms as they arise. External heat. Atropine. Stimulants.

COLLINSONIN

Standard granule—gr. 1-6, Gm. .01.

Collinsonin is a concentration from Collinsonia Canadensis, stone-root. The composition of this remedy has never been studied, except that Lochman found in it a volatile oil.

Therapeutics.—Felter and Lloyd consider it alterative, tonic, stimulant and diuretic, acting principally on the veins and mucosa, but sedating irritation of the vagus. Minute doses of the green plant cause prompt emesis. Poultices of the leaves have been applied for a great variety of affections, external and internal. It has been given for the whole line of uterine maladies, amenorrhea, dysmenorrhea, menorrhagia, vicarious menstruation, prolapsus uteri, leucorrhea, threatened abortion, and even pruritus vulvæ, dependent on varicosities. It is an old remedy for gravel, useful in cystitis, spermatorrhea and varicocele when accompanied by piles. All catarrhs are relieved by it, even the cough of phthisis. Ministers' sore throat is especially benefited by it; as are aphonia, chronic laryngitis, bronchitis, etc. In diseases of the gastrointestinal tract it relieves irritation, improves digestion, promotes the flow of gastric juice and gives tone to the weak tissues. Piles always increase the indication for collinsonin. The most marked symptoms calling for it are constriction, heat and weight in the rectum, dry scybalous feces, in pregnant women, and piles with rectal irritation but no constipation. In constipation collinsonin is useful from its tonic action on the rectal tissues.

Other conditions for which these authors recommend it are subacute proctitis, tenesmus of dysentery, dysenteric cholera infantum, rectal pain and inflammation after operations; the irritation of anal fistulas, ulcers and pockets; neurotic rectal pains, hypogastric pains not vesical, all if associated with rectal capillary congestion. In atonic dyspepsia and chronic disease with feeble digestion it acts as a tonic and stimulant, and increases secretion from skin and kidneys, relieving nervous irritation and increasing innervation (Scudder).

In chronic pulmonary diseases it relieves irritation and stimulates expectoration; quiets pneumogastric irritation, that of heart disease and the asthma attending or simulating phthisis, and strengthens and regulates the circulation. It is serviceable in hydropericardium, rheumatic heart-diseases and functional affections due to gastric irritation; mitral regurgitation and the cough of heart disease are greatly benefited by it; lack of tonicity of the blood vessels is overcome—in short, passive vascular engorgement, with dilated capillaries, torpid portal circulation and lack of muscular tonicity, call for stone-root.

Foltz advises collinsonin for ear diseases with increase of secretion but not pus, and when follicular pharyngitis or hypertrophy of Luschka's gland is present.

Scudder gives as indications for collinsonin: A sense of constriction with irritation in throat, larynx or anus; or with tickling in throat, cough on talking; sense of foreign body in rectum with contraction of sphincter and contracted and painful perineum.

Ellingwood ranks collinsonia among the stomachics, and attributes to it a tonic influence over the heart muscle, the walls of the veins and dilated capillaries. He terms it a specific for hemorrhoids, which if recent can be cured in three days to a week by collinsonia. He combines it with hamamelis, and gives them before and after operations for hemorrhoids. Collinsonia is of value in the hemorrhoids of pregnancy; also for rectal pain from any cause; it is specific for pain in the lower bowel, persistent and steady. In bladder affections it is only useful when the walls are relaxed and distended. In bicycle heart it is useful, with cactus. In passive hemorrhages also he gives it with hamamelis.

Shoemaker recommends collinsonia as a useful local astringent; as a stomachic tonic in alcoholism, lessening the appetite for liquor; as an antispasmodic in croup and whooping-cough, chorea, anal sphincter spasm with hemorrhoids, etc.; some cases of dysmenorrhea, for which he advises this remedy for a week preceding and

during the flow; in vaginal suppositories for vaginismus; for renal and biliary colic; infantile and flatulent colics; in acute cystitis, with aconite and morphine, it is more rapidly efficacious than any other treatment. For incontinence of urine in children, and when in adults there is a dripping of a few drops of urine after urination is apparently concluded, collinsonia relieves effectually. It arrests the discharge of chronic gonorrhea when the customary remedies fail. It has also succeeded in curing leucorrhea and prostatorrhea.

From this we gather that collinsonin is an astringent, specially affecting the veins and capillaries as hamamelin does. But there is more than this in it—tannic and gallic acids do not give the effects detailed. The hint as to its use in the elderly bladder is important. It may aid in postponing catheter life somewhat.

The dose of collinsonin is gr. 1-6 to iv, every two hours. The galenic preparations are so variable that it is impossible to give an approximation to their dosage. Webster prefers a tincture of the green plant, but most writers use the infusion, or Lloyd's specific, of which the dose is gtt. 1-10 to 15.

COLOCYNTHIN

Standard granule—gr. 1-134, Gm. .0005.

Colocynthin, a glucoside, is derived from the colocynth, and represents its remedial powers. The yield is about 0.6 percent (Henke).

Colocynthin $C_{56}H_{84}O_2$, is crystallizable and soluble in water. In small and repeated doses it exercises without violence an action excitant and stimulant on the gastric and hepatic secretions; it provokes both the secretion and the excretion of bile, facilitates the peristaltic movement of the stomach and bowel, and in very small doses relieves flatulence. Its stimulant action extends also to the pelvic organs. It is a rapid and efficient hydragogue.

Colocynthin has for its indication conditions in which there is a necessity of rapidly inducing a derivative action over the vast intestinal apparatus, provoking an abundant and copious biliary excretion and entorrhea. It is useful in constipation and dryness of the intestinal tract, by default of the biliary secretion or paresis of the intestinal muscles; it is useful also in slight hepatic engorgement, in venous stasis of the liver from obstructed portal circulation; in slight cephalic and spinal congestions and in slight and passive dropsies. Its stimulant effect upon the pelvic organs renders it useful in paresis and vesical paralysis; in dysmenorrhea and amen-

orrhea, caused by paresis and inertia of the ovaries and uterus; but the physician should search in these cases what is wanting to the sanguineous crasis and how to prevent the disorder of the nervous and genetic systems, to bring to each special case the general modifiers and agents well-chosen and appropriate to each patient.

In acute cases as a purgative and cholagogue a granule, gr. 1-134, should be given and repeated at short intervals, being suspended on the occurrence of colicky pains, however slight, and discontinued as soon as copious stools have been obtained. In milder cases give the granules at longer intervals—six, eight or ten daily (Laura).

In small doses colocynthin is a sure and powerful cathartic, stimulating at once intestinal peristalsis, and the mucous secretion. An increase in the urinary secretion noted especially after large doses may be caused by a local action, colocynthin being eliminated by the kidneys, or it may be due to derivation: The free, watery stools it induces relieve the abdominal viscera of abnormal pressure, the renal veins are unloaded, and the movement of blood through the renal arteries allows a freer flow of urine (Van Renterghem). Hufeland counted colocynth among the most powerful of diuretics.

Sobernheim credits colocynthin with a predilection for the abdominal ganglionic system and the inferior medullary plexus. He thus explains its beneficial effects upon paralysis of the lower extremities, the rectum and bladder. This action is in part alterative, in part stimulant, and presents some analogy with that of the acrid narcotics. In fact, when we increase the doses of colocynthin we get symptoms of narcotic poisoning—heaviness of the head, vertigo, delirium, cloudy vision, deafness, etc.

Excessive doses cause small bloody stools, acute colic, tenesmus, nausea, vomiting, tension and excessive sensibility of the abdomen, complete suppression of the stools and urine, retraction of the testicles, priapism and death (Gubler).

On autopsy we find signs of gastroenteritis, and traces of inflammation of the liver, spleen and kidneys.

The action of colocynthin is chiefly manifested in the large intestine, the colon rather than the rectum. It stimulates the secretion of bile more than does jalap or croton oil (Rutherford).

Given in fractional doses colocynthin does not exhibit the drastic action of large doses. Given in doses of gr. 1-30 to 1-20, three times a day, it incites the physiologic action of the colon; repeat these doses more frequently and it cause hyperpurgation, accompanied by painful griping.

Colocynthin is too bitter to be given in solution. It is not suitable for chronic constipation, as if long administered or in excessive doses it may occasion ulceration of the bowel. Large doses may cause collapse in feeble patients.

Felter and Lloyd say that its irritant action on the rectum may extend to the uterus, and provoke menstruation. Dissolved in whisky it has cured gonorrhea. Colocynth is purgative even when applied to the surface of an ulcer or blister. The true use of colocynth, however, is not as a cathartic but as a remedy for visceral pain. The pain calling for colocynth is cutting, darting, cramping or tearing. The dose employed here should be very small. It is of great value in stomach and intestinal disorders with sharp "belly-ache," even when rheumatic, especially in neuralgic pains of the viscera. The patient is cold, weak and faint, the sharp pain causes him to flex the body on the thighs. The back, joints and bones feel stiff and bruised, and the pain is increased on motion. Colocynth is an important remedy in dyspepsia, bilious, with bloating, and sharp pains about the umbilicus. Flatulent, worm and bilious colics are relieved by small doses. It relieves other maladies presenting the above symptoms such as cholera infantum, chronic diarrhea with slimy stools and distention, that from improper or too much food, dysentery with tormina and tenesmus, liver disorders, chronic constipation, headache, all with the characteristic pains. It relieves neuralgias of parts supplied by the solar plexus, neuralgic colic, ovarian neuralgia, orchialgia, sciatica and neuralgia of the fifth—if the characteristic pain is present. This is true of rheumatism and lumbago. When colicky pains precede or accompany amenorrhea and pressure gives relief, colocynth is the remedy. If it helps at all it helps quickly.

Specific Indications.—Pain of a cutting, twisting, boring, griping, contractive character, if gastrointestinal, then accompanied by an impulse to go to stool; colicky pains in the umbilical, iliac and hypogastric regions; dysentery with tormina in the right iliac or diffused; diarrhea with shining mucoid stools and tenesmic colicky pains; constipation with dry scybala and sharp griping pain in the lower bowel; flatulent eructations and discharges; tensive rheumatic pain with contractions; visceral neuralgia of cutting character.

Ellingwood adds the recommendation of colocynth for acute cutting pains in the stomach and bowels of infants otherwise well, intestinal derangements denoted by screams and sharp crying in sleep, persistent crying with drawing up of legs in very young babes.

The eclectic employment of colocynth is evidently founded on homeopathic applications.

Therapeutics.—Colocynthin is used as a hydragog, being usually combined with others of this group; and for dropsies due to retention of abdominal glandular secretions or to portal obstruction, especially when attended by chronic nephritis. In small doses it is useful to favor the action of colon digestion. The usual dose is gr. 1-30 after meals. It acts when given hypodermically or intravenously, and in the latter case too large doses may cause nephritis. In fact, this is said to occur when this drug is inhaled in the process of manufacture.

The powerful derivation by colocynthin may be utilized to relieve the hyperemic brain. When sciatica, ovaralgia or other pelvic pains are due in any part to a loaded bowel, colocynthin will give relief. It may be given in enema and acts well thus with no local irritation.

The griping caused by colocynthin in large doses may be prevented by giving with it atropine and aromatics. A good prescription is colocynthin gr. 1-33, atropine gr. 1-250, and capsicin gr. 1-67, after each meal.

Some day it will be found that no two agents possess exactly the same powers, or act on precisely the same parts of our organism. It has long been known that we get a better effect from a union of cathartics than from any one alone, no matter how large the dose. The compound cathartic pill has held a high place and still holds it, despite the host of rivals pushed commercially. A moderate dose of colocynthin, with euonymin, iridin, leptandrin, juglandin, hyoscyamine and menthol, will give more satisfactory results as a general cathartic than any one of these agents alone.

CONDURANGIN

Standard granule—gr. 1-67, Gm. .001.

The discovery of the remedial properties of condurango is attributed to an Indian woman. Her husband was affected with cancer; and desiring to get rid of him, she administered a decoction of condurango bark. Instead of killing him, however, it cured his cancer.

The plant is a vine, resembling the grape, but growing to enormous size. Ten varieties were described by Ruschenberger, of which but one, Condurango blanco, is credited with remedial properties, and this is official in Germany.

In 1871, Drs. Caecares and Eguiguren, of Ecuador, where the plant is found, advocated it as a remedy for cancer, syphilis and scrofula. The Minister of Ecuador to the United States brought it to the notice of the United States State Department, under whose auspices an investigation was made of the bark and its properties. The mother of Vice-President Colfax was alleged to be cured by condurango; and this, with the endorsement of some prominent physicians, aroused a whirlwind of enthusiasm over the drug, which was sold at the rate of $100 a pound. Under the stimulus of this price the population of Ecuador gathered the leaves of every plant known as condurango, and shipped the worthless truck to this country. The result was inevitable. It failed. Adverse reports came in; Mrs. Colfax died of cancer, and the alleged remedy fell into such disrepute that its use ceased entirely in America.

Nevertheless, in Germany some quiet observers asked the question: "What after all was there in condurango to give it such a reputation?" To their efforts to answer we owe the data presented.

In Ecuador numerous plants employed as remedies for cancer, snake-bites, and syphilis, are called condurango. The true bark is probably derived from Gonolobus condurango triana, of the Asclepias family. Two or more glucosides, possibly an alkaloid, and one or more resinoids, have been found in this bark, the separation of which entails great difficulties. Antisell, Flueckiger, Schmiedeberg, Jukna, Vulpius, Reuter and Carrara, have investigated the chemistry of condurango, with varying results. The latter isolated in 1892 two bodies: Soluble condurangin, $C_{20}H_{32}O_6$, and insoluble condurangin, $C_{18}H_{28}O_7$.

Physiologic Action.—Studies have been made with Vulpius' condurangin and Jukna's resin glucoside which act alike, the resin being somewhat stronger. Their effect is most marked on the central nervous system. Small doses disturb coordination, the movements becoming ataxic, with great debility and marked impulse to move about. Respiration and pulse are unaffected, the pupils normal, the tendon and cutaneous reflexes somewhat heightened. The appetite is diminished or stopped. Salivation and emesis are frequently seen.

Large doses excite primarily, and paresis ensues. There is a peculiar stiffness of the extremities. Violent cramps follow, at first tonic, then clonic. Respiration becomes shallow, the pulse rapid, the stiffening relaxes, the cramps subside, and paresis supervenes. Consciousness and sensation seem to be unaffected. The pupils dilate during the cramps, but are normal in the intervals. Respira-

tion is retarded and superficial, the pulse small, and death occurs during a convulsive spasm, or from prostration, presumably from respiratory paralysis. The cramps are due to action on the cerebral and medullary centers, and may be checked by chloroform, chloral, morphine or curarine. The vomiting is also centric and not reflex. Condurangin does not influence the heart, the arterial tension or the intestinal muscular fiber. Direct contact with voluntary muscle, or with motor nerves, at first increases the electrical irritability, which soon subsides and finally ceases.

Nothing characteristic is found on post mortem. The lethal dose for cats or dogs intravenously is Gram 0.02—0.03, per kilo-weight. By the stomach the lethal dose would be Gram 0.040—0.048 per kilo. To kill rabbits the dose is Gram 0.03.

It is evident that as yet nothing has been shown by these studies to in any way clear up the question of the use of condurango in cancer; which must be decided by purely clinical evidence. A summary of this evidence we present.

Therapeutics.—Wilhelmy gave condurango in six cases of gastric and one of œsophageal cancer. Under its use the pains were materially reduced after the drug had been taken one or two weeks; the appetite improved, vomiting decreased, and in three cases there was a gain in weight. All but one died, though material relief had been afforded.

Hoffman obtained similar benefit in 132 cases. *In pyloric cancer it was found that prolonged contact of the drug with the stomach walls was advisable.*

In gastric ulcer brilliant results followed the use of condurango and iron, especially when anemia preceded the malady. In twenty-seven cases absolutely diagnosed (hemorrhagic, etc.), this treatment was used. Pain and hemorrhage ceased usually in four days. The drug was continued two months. Relapses were mild and soon over. In anemia this combination acted better than iron alone. In acute and chronic gastric catarrh good results were obtained.

Riess reported in fifty cases of dyspepsia, catarrhal or with dilatation, that condurango gave no advantage over ordinary bitter stomachics, if it were as good. In carcinoma, not gastric, striking benefit was rare. In thirty cases of peritoneal carcinoma, primary cancer of the gall-bladder, or large hepatic metastases, except a transient improvement of appetite and easing of pain there was no benefit. In eight cancers of the œsophagus, the dysphagia and cachexia were eased doubtfully—diet and sounds may have been the true sources of benefit.

Of pure gastric cancer, with anorexia, dyspepsia, vomiting, hematemesis, cardialgia, progressive cachexia and in time palpable tumor, he reported 120 cases observed personally and records covering 800. In none was the drug without effect. Even when not used until the last stages, in the last weeks of life, the appetite improved and euphoria occurred. The effect is far more striking when the drug is given four weeks. It is readily taken, well borne, without repugnance, for very long periods, to the amount of 10.0 Grams of decoction a day.

In a few days the appetite increased, nausea disappeared and vomiting lessened and ceased if not due to stenosis of the pylorus and ectasia. In eight to fourteen days gastric pains lessened with hardly an exception, and finally disappeared almost completely. Assimilation improved with nutrition; the patients felt better and grew stronger, often weighed more. In most cases life was prolonged.

Of 108 cases without condurango, 70 died, 28 left unhealed, 10 left improved. Of 20 cases treated with condurango, 10 died, 2 were discharged unhealed, 8 improved.

Of 80 condurango cases the average duration of treatment was 43.4 days. Of these 66.3 percent died, on an average in 39.5 days; 33.7 percent were discharged after an average treatment of 54.8 days, 24 as improved and 3 cured.

Of 116 cases treated without condurango, the average duration of treatment was 21.2 days. Of these 92.2 percent died, average 22 days; 7.8 percent were discharged, average 11.7 days' treatment, 5 improved, 4 not cured.

Of 64 cases in which a palpable tumor was demonstrated, a distinct decrease in its size could be shown, resulting in complete or almost complete disappearance. In all the rest the growth of the tumor ceased. *An increase in size of the tumor was never observed during prolonged condurango treatment.*

In three cases (two discharged as improved, one as cured) autopsies were held for death due to other causes, soon after their discharge; and the autopsy confirmed the diagnosis and the cure. In other cases the tumor decreased in size for a time but the improvement ceased, and at death the autopsy confirmed the diagnosis.

Summary: In some cases condurango completely cures gastric cancer and other gastric maladies; in many more it causes a permanent substantial improvement of all the chief symptoms, dyspepsia, vomiting, cardialgia, cachexia and tumor, and prolongs life. In the rest it caused at least transient improvement and euphoria.

Binz recommends in cancer or its suspicion, the steady use of condurango. *The effect invariably is distinctly local.*

What other remedy affords as much benefit in cancer of the stomach?

Careful study of Riess' report fails to show any reason to doubt the correctness of his diagnoses, nor that some cases of gastric cancer were undoubtedly cured by the internal administration of condurango. But the effect was distinctly and invariably local; and here we wish to make our chief point. Seemingly it has occurred to no one to use any of the bodies derived from condurango hypodermically, injected into the cancerous tissues. And yet it is evidently the step to be next taken; and surely it is worth while!

The effects of condurango in gastric ulcer are also notable; but there are other remedies for this malady, whereas in cancer we are assuredly in need of more effective weapons than those now in use. So also in other gastric maladies, there has not as yet been shown any good reason for substituting condurango for the prevailing treatment.

Riess gave condurango in decoction, 10 to 20 parts in 200, a tablespoonful several times a day. Condurangin separates by heat and redissolves on cooling; so that the decoction should not be filtered until cool.

Dr. W. K. Clark reported a case in which an exploratory incision was made and revealed a carcinoma, completely enveloping the pylorus. The wound was closed and the patient left to die. He put her on fluid extract of condurango, beginning with half-dram doses, gradually increasing until within a month she took two drams every four hours during the day. By the time the wound was healed so that the patient could leave her bed, she could eat anything she wanted and was gaining flesh daily. She continued taking condurango for six months, the dose finally being reduced to a teaspoonful three times a day. At the end of six months she was apparently well, and three years afterwards the doctor reported his patient, who was his own mother, as living and enjoying the finest health, her digestion being better than it had been for ten years.

A patient reports:

"I presume you remember me, as having called at your office with a letter from Dr. ——— of this place.

"I am now very happy to be able to state that Dr. ——— congratulated me yesterday for being the first person cured of cancer in the throat. Of course, the compliment was returned to the doctor who performed the cure, and to your kind advice, which may enable

this old Dutchman to live many years yet, to thank you a thousand times for your life-saving advice."

His doctor writes:

"I am glad to inform you that my friend and patient, Mr. ——, is well, for which he seems to be the happiest man in town. I began injecting 1-67 grain of condurangin twice daily in the center of the sore, May 13, and increased to 1-16 grain, followed by 10 minims of nuclein solution, after which I applied 5-percent methylene blue. I also gave nuclein solution and condurangin internally three times a day. I hope this cure will be permanent."

This patient subsequently died from a cancer developing beyond the reach of treatment. The original growth was contracted and obsolete. The new growth appeared to be distinct from the first one.

"I was called two years ago to see a man seventy years old who had been suffering from cancer of the stomach for two and a half years. He had almost starved to death, as he could not retain food more than half an hour at any time except meat broths or very thin soup. He also suffered very excruciating pain for hours after vomiting food and nothing but cocaine or morphine seemed to give him any relief. Condurangin relieved the pain entirely and he gained five pounds in weight, but died in a few months."

Condurangin has been shown to be remarkably efficient in subduing gastric pains. Dismiss for a moment the question of whether it is curative in gastric cancer, and whenever you have a case in which there is pain, hyperesthesia, in the stomach, which needs to be quelled; after ridding this organ of any local cause which may keep it up, such as the presence of an excess of hydrochloric acid, try the effect of a milligram of condurangin dissolved in a tablespoonful of hot water, taken one hour before each meal and on going to bed. The writer has had but few cases in which to try this suggestion, but in each of these he has found within forty-eight hours that there was a distinct benefit accruing, the oversensitiveness subsiding and the patient finding himself distinctly and decidedly relieved.

Merck lists condurangin, a mixture of the glucosides. It is an amorphous yellow powder, of aromatic bitter taste, soluble in alcohol, water and chloroform. Dose Gram 0.0065 to 0.016 three times a day (gr. 1-10—1-2). We would recommend Gram 0.001 (gr. 1-67) as the beginning dose hypodermically, rapidly increased to Gram 0.005 or more, in watery solution, injected into the substance of any cancerous tumor in reach.

CONVALLAMARIN

Standard granule—gr. 1-12, Gm. .005.

From the lily of the valley are derived two glucosides, convallarin, a cathartic, and convallamarin, on which the heart tonic virtues of the plant depend. This principle closely resembles digitalein, being freely soluble in water.

Lenneker reports his conclusions from a very extensive and successful experience with convallaria extending over five years. He employed this drug in all heart affections, excepting fatty degeneration. In the latter convallaria proved injurious. Convallaria is one of the remedies giving tone to the stomach, increasing appetite and exerting a tonic effect on the intestinal mucosa, increasing the action of the bowels in many. He quotes one case of cardiac disease, from the use of tobacco, in which digitalis had failed to give relief, although pushed. He prescribed convallaria and nux vomica with excellent effect. The use of the two remedies at once unfortunately vitiates his conclusions.

Convallamarin has a retarding influence upon the heart, increasing the amplitude of its contractions, and slightly reducing the blood pressure. In toxic fatal doses it arrests the cardiac action in systole. The secondary actions of convallamarin are slight purgation, and an increase of the salivary and urinary secretions.

The juice of convallaria was used by M. Laigre (*Th. de Paris*, Juillet, 1903). He obtained it from the entire plant gathered before its flowering, and had it so that one cubic centimeter of the juice represented exactly a Gram of the fresh plant.

The extract of convallaria is mixed, impure, for while the flowers of the plant are rich in convallarin they contain also a small quantity of prussic acid. This fact forbids the giving of it exclusively. The extract made from the rhizome of the plant has emeto-cathartic properties highly accentuated. The extract from the leaves is three times less active than that made from the entire plant. It is on this account that the last is given the preference, for its certainty of action and constancy. In the manufacture of the extract the proportions taken are: two-thirds of the flowers and stems and one-third of roots and leaves.

The divergence which clinicians, who studied this plant, show in their advices seems to be owing principally to the inconstancy of the preparations of which they made use.

An excellent succedaneum of digitalis, convallaria can be given in the periodical intervals of the former, or altogether instead

of it, when the foxglove has failed to do any good. Convallaria is better tolerated than digitalis, is not cumulative, does not increase the blood pressure, and is slightly laxative, and its effects while they are mild are nevertheless not transient. The slight irritant action which this plant was noticed to have on the kidneys will necessitate a looking after the urine from time to time as it should not be given to albuminurics. It is not advisable in infantile therapeutics.

Physiologic Action.—Marme has made the following summary of the action of convallamarin upon the vascular pressure:

1. The normal arterial pressure is augmented, generally with slowing of the pulse.

2. This increased pressure continues while the pulse becomes faster than normal.

3. The pressure continues high while the pulse becomes irregular in frequency and in force.

4. The pressure falls swiftly, the heart is arrested, and the subject dies.

The action of convallamarin is especially directed to the heart and is according to Boehm absolutely independent of vasoconstriction from excitation of the vasomotor nerves.

Van Renterghem records the following observations made on his own person with Merck's convallamarin.

The first day he took gr. 1-12 every half-hour till 20 doses had been taken. No effect was manifested except that by evening the pulse was more developed. Next day the dose was doubled. In the afternoon, rattling in the stomach; in the evening two soft stools, no abdominal pain—that day he had taken no saline in the morning. The pulse was 82 in the morning, 80 at 10 p. m. During the night, one soft stool.

Third day: Took gr. 7 1-2, between 11 a. m. and 9 p. m. The pulse gained in energy but the rate was unaltered. Digestion was unaltered except for the increased peristalsis.

During the day there were five small stools, in the evening some abdominal pains; during the night two more stools. Next morning he took a saline, as in spite of the laxation he felt some toxemic fever. The pulse was more forcible than usual and the rate was up to 110. Temperature 99.3, heart and temples beat strongly; slept. Awakened at 1 a. m. by a violent peal of the bell, he was obliged to go in a carriage a quarter of an hour, during a "time of ice," for a laborious confinement ended by the forceps. The duty was performed with difficulty; the traction fatigued beyond measure and

caused nausea with difficulty restrained. The heart and arteries beat strongly and more frequently. By 7 a. m. the rapidity of the pulse had lessened; at 8 two good stools and sufficient urine, after saline. At 9 a. m. *cafe au lait.* The pulse was perfectly calm and had fallen to 80. No abdominal symptoms.

His conclusion was that doses of gr. 1-12 to 1-6 every hour do not lessen the pulse rate, but increase its force with the increase of arterial pressure. Doses of gr. 1-3 to 2-3, repeated, produce the beginning of paralysis of the pneumogastric nerve, as shown by feverish rapidity of the heart beats. No marked effect was noted on the renal functions. The drug evidently did not accumulate in the body.

Shoemaker says that convallamarin sometimes causes hemoptysis, dyspnea and other disagreeable symptoms.

Therapeutics.—Convallamarin has been used in heart diseases, especially those of the mitral valve. When compensation fails it strengthens the heart, increases the excretion of urine, and quickly relieves dyspnea and palpitation. In angina pectoris and functional affections of the heart it has also proved beneficial.

Janowski recommended it in renal and cardiac dropsies. In cirrhosis of the liver it acts as a diuretic. In chronic nephritis it strengthens the circulation, relieves dyspnea, increases the urine, reduces dropsy and lessens albuminuria (Shoemaker). We may doubt whether its occasional good effect in asthma is due to a relaxation of arterial spasm. More likely it is in cardiac asthmas that convallaria finds a place.

It is sometimes useful in neuralgias, insomnia, and to quiet the restlessness of fever. The palpitation and dyspnea of febrile phthisis are mitigated by it.

Sée valued convallamarin above all other remedies, even digitalin, in cardiac dropsies.

King gives as specific indications for it: Heart irregularities due to mechanical impediments; mitral insufficiency; dropsy of cardiac origin; palpitation and vehement heart action, with arrhythmic movements, dyspnea and diminished arterial pressure; quickened pulse with capillary obstruction.

The therapeutic applications of convallamarin are those of digitalin. The former may be preferred when the latter through idiosyncrasy is not well borne; or when the menace of collapse defies digitalin. Here strychnine, caffeine, or even atropine in small doses, has an urgent and legitimate indication. Digitalis and its official preparations should be proscribed, or employed only

with the greatest prudence and incessant vigilance, since they may produce, besides gastric and cerebral troubles, collapse and even an arrest of the heart, prolonged and perilous (Laura).

"Convallamarin is indicated in organic cardiopathies with arrhythmia and failing compensation, especially in lesions of the orifices and the valvules. It is especially indicated in regurgitation of the tricuspid and in insufficiency of the mitral. By rectifying the heart-action and consequently the flow of blood in the greater and the lesser circulation, it ameliorates with rapidity the respiratory, cerebral and renal functions. In general this remedy may be described as a succedaneum of digitalin, in some cases usefully replacing it." That is all that Laura will say to its credit; but the Italians as well as the French have for many years adhered to their digitalin as the one perfect representative of digitalis, and felt that they had no occasion to look further.

The dose of convallamarin according to Laura is for an adult 1-12 to 1-6 grain; rarely more, large doses causing toxic phenomena.

Convallamarin itself does not act on the bowels but convallaria does; this advantage however, if it be one, is overbalanced by the exceeding variability in strength of the extracts found in the market. Moreover, as this drug is costly and rarely employed, the chance of obtaining an extract that has not decomposed is very small. If one desires to employ this agent, the granules made with milk sugar as the excipient preserve the contained glucoside without change for many years. The writer has in his cabinet granules of convallamarin made by a pharmacal company, that ceased active work fifteen years ago, and these granules being recently tested, displayed full and unimpaired activity.

The place of convallamarin may be summed up by saying that it replaces digitalin in the whole line of its action and uses, but does not unsettle the stomach as the foxglove sometimes does, and acts on the bowels slightly. When of good quality it may be used as an alternant with digitalin. But we have found no evidence to show any further applications in therapeutics.

COPPER ARSENITE

Standard granules and tablets—gr. 1-1000, Gm. .0000625; gr. 1-250, Gm. .00025; gr. 1-100, Gm. .000625.

Copper arsenite is a valuable intestinal disinfectant. It is toxic in overdoses, causing heat and irritation as do other forms of arsenic, particularly manifest in the duodenum where it exercises

its special activity, and in the small intestines generally since the drug is here principally eliminated. It is then reabsorbed by the glandular apparatus, whose cells will be irritated if the dose is too large. Medicinal doses stimulate these cells and restore their functional activity. By this means the absorption of toxic materials is hindered and normal elimination favored.

The rôle of copper arsenite therefore differs radically from that of the ordinary intestinal antiseptics, in that the former does not act as a chemical disinfectant, nor as a germicide, but is rather a stimulant of the functions of the gland cells of the gastrointestinal mucous membrane. Its place is therefore after the alimentary canal has been cleared by calomel and saline, and the fetidity of the stools removed by the sulphocarbolates. The restoration of the secretory function is then indicated, and completes the cure. For this purpose copper arsenite has approved itself as remarkably effective. It is recommended in a very wide range of diseases, even as an antiseptic in typhoid fever, cholera infantum, etc.

When there is fermentation in the stomach or duodenum, first clear the bowels and then copper arsenite will put an end to the nausea, pain and diarrhea very quickly. When there is pain immediately after eating, indicating stomach indigestion, or several hours after meals, indicating intestinal indigestion, copper arsenite taken before each meal will give prompt relief.

Shaller describes his first case treated by this remedy—a child with cholera infantum, profuse diarrhea, constant vomiting, emaciated, almost in collapse. Improvement was manifest within two hours, after commencing with this remedy, and recovery ensued. His experience is so typical of what occurs when an old and successful physician first lays aside his tried methods to experiment with a new one that promises better things, that we will quote it here verbatim:

"It must be confessed that the writer felt extremely uneasy in leaving this patient in such a dangerous condition and prescribing only 1-500 of a grain of copper arsenite. It seemed as if this small dose could not possibly bring relief in so serious a condition. After passing two very uneasy hours, the patient was again visited, I thinking that possibly the child was dead, and if so it had died simply because active, substantial treatment had not been given. After treating many cases by well-established methods in Cincinnati at that period, when cholera infantum was extremely common, giving tangible doses, it seemed almost like murder to turn around and give only 1-500 of a grain of copper arsenite.

"Considerable relief was expressed when the patient was found alive; utter amazement was experienced when it was learned that by giving so small a dose actual improvement had occurred. Vomiting and stools were less frequent, and some general improvement was manifested which continued and the child made a complete recovery.

"Probably all physicians feel just this way when changing from old ways with single large doses to the newer way—to this only way; to what appears to be extremely minute, almost infinitesimal and inadequate doses. Yet it is a fact easily verified that apparently minute doses, frequently repeated to effect, cure. Everything in dosimetric medicine tends to prove this. Strong prejudices in favor of large doses, and old favorable methods, rooted deeply, must all give way to the certain and prompt response following small doses frequently repeated."

Arsenic in very small doses has been recommended as a gastric sedative in many conditions, such as the vomiting of pregnancy and the morning sickness of drunkards. There is no other arsenical preparation quite so effective as the copper salt in such cases. The small dose and lack of unpleasant taste gives it a great advantage.

The average dose of copper arsenite is from gr. 1-250 to 1-100.

This may be given every half-hour in acute gastric irritations, or before meals in chronic cases. Irritation or pain following it indicates smaller doses, and benefit will often follow doses of gr. 1-1000, frequently repeated. To infants the latter dose may be given every half-hour or less frequently. Shaller strongly advises that this remedy be given in solution.

The only indication of action is usually the subsidence of the pain, nausea and diarrhea, and the improved condition of the stools. Irritation of the stomach indicates toxic action, but it does not imply that the remedy has been ill-chosen, but, rather, that the doses have been too large. Keeping just below the irritative point usually gives the most decisive therapeutic effect—the small dose frequently repeated until the desired result is produced. In many cases it is a decided advantage to give a glass of hot water with a scruple of baking soda an hour before food is taken, and the copper arsenite half an hour later, when the remedy may obtain access to the cleaned surface of the diseased mucous membrane, and be out of the way by the time food is to be introduced. Most of the arsenic given is wasted by neglect to administer it scientifically: If taken after meals it is mostly converted into iron arsenate, which is almost insoluble and is discharged in the stools. Bartholow pointed

out that persons who could take twenty drops or more of Fowler's solution after meals could not take more than a drop or two before meals.

Aulde advocated copper arsenite as a remedy for seasickness, in doses of gr. 1-100 before meals. The writer has found this suggestion of value, especially when the bowels have been thoroughly cleared and the diet regulated, adding hyoscyamine or atropine enough to secure a slight but sustained effect. It has been suggested that dilute hydrochloric acid be added to the water used in dissolving copper arsenite, for local or hypodermic use; the result is a chlor-arsenite of copper solution, which is stable. One grain of copper arsenite in four ounces of water, to which the acid is added drop by drop until a clear solution results, will give a solution of which thirty minims will equal gr. 1-65. This dose is recommended—hypodermically exhibited every second day—in typhoid fever and in tuberculosis. Abscesses do not follow. In aphthæ and stomatitis a solution of copper arsenite may be used locally, and a spray of the above strength is said to be effective in the asthma which accompanies hay fever.

In some bilious attacks gr. 1-1000 in hot solution will, if taken at one-fourth to half-hourly intervals, prove almost a specific. The indications are dizziness, flatulence and alternating constipation and diarrhea.

For gleet a solution of one grain to four ounces of water (with the addition of hydrochloric acid) will prove beneficial; the irritability of the urethra is lessened and the disease cut short.

One full dose, one granule gr. 1-100, followed at fifteen-minute intervals by small doses, gr. 1-1000, will stop nausea promptly, except perhaps in that caused by cirrhosis of the liver. In nearly every case copper arsenite is best taken in hot solution, and in infantile diseases the small dose, gr. 1-1000 frequently repeated, will prove of most benefit.

In all internal use of copper arsenite, as improvement is manifest the doses should be diminished in frequency, or decreased in strength, or both. Thus given, there is no safer remedy in use; and its marked effectiveness in the tiny doses recommended has been the means of convincing many of the utility of the small and frequently-repeated doses, leading them to an investigation of the merits of and the ultimate adoption of alkaloidal or active-principle (small-dose) methods.

The greatest difficulty in the way of beginners with this remedy is that they have been led by too enthusiastic reports, and by ignor-

ance of the proper method of utilizing the medicament, into too great expectations as to its "marvelous" powers. Miracles are scarce in these days; and the principles of a correct routine are not to be dispensed with for any remedy. Little opportunity has copper arsenite to display its virtues if given while the bowels are encumbered with pounds of decomposing feces, the blood entoxined by a flood of poisons therefrom. First completely empty the bowels, and establish an aseptic state there; then such remedies as this may be studied intelligently. The frequent iteration of this advice will indicate to the reader how often its need has come to the writer's notice.

J. F. Stevens reports 43 successful cases of typhoid fever treated by the use of copper sulphate as an antiseptic.

CORNIN

Standard granule—gr. 1-6, Gm. .01.

Cornin is a concentration from the Cornus florida, or dogwood. Geiger obtained from this bark a bitter crystalline principle, cornine; soluble in water and alcohol.

Felter and Lloyd state that dogwood is tonic, astringent and slightly stimulant. It has been much used as a substitute for quinine in ague, and in typhoid fevers. It increases the strength and frequency of the pulse, and elevates the bodily temperature. It relieves quinine headaches, pyrosis and general exhaustion.

Specific Indications.—Tonic antiperiodic, in intermittent and miasmatic fevers; pyrosis; quinine headache; general exhaustion; feeble relaxed tissues; feeble pulse and subnormal temperature; quinism.

Ellingwood advises cornus for atony of the gastrointestinal glands in malaria, and to antidote the malarial poison; increasing appetite, it improves digestion, relieves drowsiness and dullness following imperfect digestion; also improves intestinal digestion.

This meager account gives very little information as to this remedy, which we are convinced is worthy of extended investigation. For some years the writer has given cornin for weakness of the erectile tissues, and believes it the best remedy for this condition yet introduced—far superior to yohimbine. The effect of cornin is that of a tonic, slow to be manifested but enduring long. The dose for this purpose is a grain four times a day, and it should be continued for at least a month. It is by no means a cure-all, for the condition may depend on any one or more of several pathologic

elements, and each case requires study. With many men the restoration of power is followed by renewal of the excesses that first induced the exhaustion, and this obviously will not be, and should not be, cured by any treatment. But cornin is a valuable agent in restoring erectile tissue when not entirely beyond the reach of remedies.

This points to the probable value of cornin in other forms of debility, and altogether this agent deserves study at the hands of those who do not consider the whole story of the tonics comprised by iron, strychnine, quinine and cod-liver oil.

As a remedy for ague cornus was employed largely in the South during the civil war, and gave satisfaction. But the crude preparations alone to be had were brought into competition with the modern representative of Peruvian bark, quinine, and obviously only decided superiority could overcome such a handicap. The crystalline cornine should be isolated and tested fully by modern methods.

CORYDALIN

Standard granule—gr. 1-6, Gm. .01.

Corydalin is a concentration from the tubers of Corydalis formosa, the turkey corn. The plant contains an alkaloid, corydaline, discovered by Wenzell. It is insoluble in water, soluble in ether easily, in alcohol with difficulty. Merck describes three alkaloids found in this plant. By the eclectics corydalis is accredited with tonic, diuretic and alterative properties. It was employed as a remedy for syphilis but except as a tonic is not thought to possess any value (King). When syphilis is constitutional, in debilitated subjects, corydalis possesses an efficacy unequalled as an alterative tonic (King). Recent syphilitic nodes, especially on the skull, are chiefly influenced by it. It promptly relieves the shin pains. Locke recommends it in atonic, scrofulous and syphilitic cases of amenorrhea, dysmenorrhea and leucorrhea; also as a digestive tonic in atonic abdominal enlargement, dysentery and diarrhea with coated tongue, fetid breath and poor digestion. It is useful in malarial cachexia.

Specific Indications.—Syphilitic or scrofulous diathesis; yellow skin with lymphatic enlargements; syphilitic nodes; increases waste and improves nutrition.

Ellingwood says overdoses cause biliousness, deranged stomach, excessive secretion of mucus, gastrointestinal catarrh, anorexia, indigestion, fetid breath, irregular bowels, colic, and malaise. In

remedial doses it is a tonic, increasing vitality and influencing metabolism; cooperating with echinacea, berberis, hydrastis, xanthoxylum and stillingia. In chronic skin diseases with marked cachexia it is speedily curative; superior if there is relaxation of tissue and plethora.

The dose of corydalin is a grain four times a day in chronic conditions.

COTOIN

Standard granule—gr. 1-67, Gm. .001

Cotoin is a glucoside derived from the bark of an undetermined South American tree. It is soluble in alcohol or ether, or in boiling water, almost insoluble in cold water. Watery solutions of alkalies or of their carbonates dissolve it.

Coto has the properties of a bitter tonic and of an astringent. It has been used with success as a remedy for various forms of diarrhea. Burkhart and Rieker attributed to it extraordinary efficacy in enteritis, diarrhea, dysentery, etc. In cholera infantum it acts as other astringents do. In phthisis it is more effective, and also restrains the colliquative sweats. Engel asserted that it had a selective action in tubercular diarrhea, so that any diarrhea checked by coto might thereby be diagnosed as tubercular. Cotoin is especially useful where opiates are contraindicated.

Large doses of coto cause a sense of warmth in the stomach, and larger ones give rise to nausea and vomiting. The saliva is increased. It retards the development of bacteria, and of putrefaction. It actively dilates the intestinal vessels. In healthy persons it does not constipate. Shoemaker pronounces coto remarkably efficient in all forms of diarrhea except that with intestinal ulcers.

Albertoni reported no success in drunkards or when the portal circulation was obstructed, as in cirrhosis. Enteric hyperemia and tendency to intestinal hemorrhage contraindicate coto. In acute intestinal catarrhs it should therefore be used with care.

Coto is singularly repugnant to the stomach, and few patients will take it long, the aversion becoming insurmountable (Huesemann).

Cotoin does not interfere with the action of pepsin or of ptyalin. It is excreted by the kidneys and diminishes the excretion of indican. Insoluble in the gastric juice it passes unaltered into the intestine. The intestine, says Albertoni, is the habitat par excellence of the putrefactive process. Here we encounter nearly all the products of

the putrid fermentation, peptones, tyrosine, leucine, organic acids, phenol, indol, skatol, ammonia, carbonic acid, sulphydric acid, hydrogen, hydrogen protocarbonate. The majority of these are reabsorbed, and traces of phenol are found in the stools, most of it in the urine. The indican of the urine is derived from the indol. The quantity of indican found in the urine shows the intensity of the putrefactive process in the bowel. Albertoni found that phenol continued to be found in the urine despite the use of cotoin. The decrease of indican observed by Burkart and Pribram under cotoin must be attributed to a secondary effect, consecutive to the amelioration of the intestinal malady. By determining active dilation of the intestinal vessels cotoin improves the nutrition of the mucosa and increases its faculty of absorption.

It follows that the indication for cotoin in diarrheas is asthenia, the atonic or relaxed condition. Van Renterghem found this agent useful for aged patients. In children the diarrhea of rickets is especially amenable to cotoin. Much larger doses than those above given may be used. Albertoni gave gr. 1-6 to a newborn infant with impunity. Van Renterghem gave to an adult ten grains within twenty-four hours.

The dose of cotoin is gr. 1-67 to 1-22 every two hours.

CREOSOTE

Standard granule—gr. 1-67, Gm. 0.001.

Despite the differences of opinion regarding the usefulness of creosote in phthisis it will continue to be given in this disease until something else has proved more efficacious. It is a powerful antiseptic, resembling carbolic acid greatly in its effect but is markedly less injurious to the human tissues. It is eliminated through the lungs and bronchial mucosa, and though it cannot possibly destroy the bacilli in the lesion, it probably renders them weaker and certainly renders the parts a less suitable field for their propagation. It also disinfects the sputum, and this is of no small moment for to render the discharges of the phthisical patient less dangerous to himself and others is to accomplish a good deal. The consumptive often reinfects himself. This is unquestionable. The drug is also eliminated through the kidneys and this has led to its use in diabetes and Bright's disease. While it is impossible to term it a remedy for these conditions some cases have improved upon it. Creosote destroys germs with which it comes in contact and thus is of use in stomachic and intestinal fermentative conditions. It is also an

excellent antinauseant. It can be given combined with bismuth in all forms of nausea with success.

The dose in phthisis should be large. Three to six granules may be given every three hours. An excellent plan is to begin with two and gradually increase as the patient becomes tolerant. Some subjects can take enormous doses and thrive upon them. The secret of success with this remedy in pulmonary phthisis is "dose enough." In purulent pneumonitis creosote will prove invaluable. Two to four granules may be given with some nutrient every three hours. In bronchitis and bronchorrhea it corrects the offensive discharges and certainly aids in obtaining a cure. In such cases as are suited to this remedy, cough lessens, sputum diminishes, night sweats cease and diarrhea (if present) stops. Vomiting is controlled, the gastric irritability lessens and the patient shows general improvement. Creosote should be given either with food or with a diluent. It is a useful and dependable remedy and should be in every doctor's case.

Sollmann sums the values of creosote: It is a standard remedy in tuberculosis. It is useful in other pulmonary diseases, especially if employed by inhalation. None is excreted by the lungs (Bufalini), but it increases the secretion of mucus and of urine, when taken by the mouth. It is an efficient intestinal antiseptic. It hastens the absorption of pleuritic effusions when rubbed over the chest. Guaiacol when thus rubbed into the skin exerts an antipyretic power not manifested when given internally. The local anesthetic power is utilized especially in dentistry.

CROTON OIL

Standard granule—gr. 1-67, Gm. 0.001.

Croton oil may be separated by alcohol into two portions, that soluble in alcohol being irritant, the residue purgative. The former depends on crotonolic acid for its effects.

Sollmann says the active principle is crotonoleic acid, existing mainly as an inactive glyceride, which is split in the intestine and becomes active.

Applied to the skin croton oil causes a pustular inflammation or eruption, sometimes leaving scars. The vapor may cause inflammation of the conjunctivæ, nose and air-passages. Burning follows its local application in five minutes. The pustules dry up and disappear in a few days. Sometimes the oil is absorbed and causes purging, even through the unbroken skin. Applied to wounds or de-

nuded surfaces it causes phlegmonous inflammation, with suppuration.

Taken internally in doses of a drop, croton oil causes burning and irritation of the mucous surfaces with which it comes in contact. Within two hours abdominal rumbling and pains begin, with watery stools that irritate the anal tissues. Larger doses cause symptoms resembling cholera morbus, violent vomiting, aching in the muscles and joints, cyanosis, fall in temperature and death. Three drops may cause violent gastroenteritis. Five drops have caused death.

Croton oil is given as a derivative in congestions of the brain or spinal cord, in threatened apoplexy, etc., and in eclampsia, where there is need of prompt and powerful action. In obstipation and intestinal obstructions it is a very dangerous drug, and does infinitely more harm than good. Better rely on small liquefying doses of salines, with alkaline enemas.

The average purgative dose is one drop. Some believe that croton oil in smaller doses acts mildly, like castor oil; and it has been given with asserted benefit in pills of soap containing each one-tenth of a drop of croton oil. The oil from which the acridity had been abstracted by alcohol might be thus used, and possibly we could thus obtain in a granule or tablet the virtues of the bulky and disagreeable but valuable castor oil.

There is a popular belief that croton oil in huge doses will cure the alcohol habit; and the writer has been asked to prescribe it in doses of a dram. In one case a woman administered to her husband half a dram each of croton oil and oil of black pepper at a single dose. It did not *quite* kill the patient, though perilously near it, and accomplished a cure. In another case a consumptive took a similar dose by mistake and recovered. In these cases it is probable that the oil was not of full strength.

Locally the oil is applied for any of the purposes for which a counterirritant may be used. The promptness of its action recommends it; but the effect lasts so long and the occasional occurrence of absorption and purgation have made this application less popular than of old. If diluted with three times its bulk of any bland oil like sweet almond oil, the effect is pleasanter and more under control. A few drops rubbed in over the sacrosciatic notch is decidedly beneficial in sciatica.

In ringworm this oil has been applied as a substitution remedy, but modern methods are better. When given as a purgative it is well to employ castor or sweet oil as a vehicle.

CUBEBIN

Standard granule—gr. 1-67, Gm. .001.

Cubebin, the resinous principle from the unripe berries of Piper cubeba, is a stimulant stomachic carminative and expectorant. The fluid preparations contain a volatile oil, a fixed oil and cubebic acid which make them somewhat more irritating to the intestinal tract than is cubebin.

Its chief use is in disorders of the urinary passages. In gonorrhea and gleet its action is well known. It acts as a sedative to the mucous coat and seems to allay irritability. The standard granule contains gr. 1-67, and one, two or three may be exhibited every hour.

As an expectorant one milligram every two hours often gives good results. Scillitin may be given in conjunction; and cubebin and codeine, one granule of each, have relieved some markedly stubborn cases of bronchial asthma. In arresting the discharge following acute prostatitis cubebin is useful and it has been recommended as a remedy for spermatorrhea. In catarrhs of the bladder it is of undoubted value; indeed, it is here that its chief field exists. It should not be forgotten that large doses sometimes cause a marked feverish condition with some erythema.

Besides the volatile oil, besides also the malate of lime, and magnesia, and besides cubebic acid, $C_{44}H_{16}O_4$, cubebs contain also cubebin, $C_{33}H_{34}O_{10}$, which last is to be regarded as the principal medicament, although other authors than Laura, from whose works this is excerpted, regard it as inert, and refer the activity of cubebs to the resin which it contains. Cubebin crystallizes in needles.

This active principle is eliminated for the most part by the urine, rendering it more abundant and more fluid. Another part is eliminated by the bronchi, and still another part perhaps by the sudorific glands by means of the sweat (Ruatta). In small doses it stimulates the stomach and intestines.

"Cubebin," says Burggraeve, "has a slight action in gonorrhea, but when administered in doses of thirty granules a day, then after a transudation of all the genitourinary tegument, the medicine exerts a remarkable action on the secretion and renders the urine more copious and less irritant. Cubebin occasions no diarrhea as copaiba does." Burggraeve enployed cubebin in gonorrheic metritis in conjunction with sodium benzoate. Laura also has employed cubebin and has verified the diuretic virtues in the absence of irritating phenomena.

The form and the administration of cubebin is the same as that of the other active principles.

Cubebin has its largest field of application in urethral catarrhs and syphilitic gonorrhea, but it is equally useful in vesical catarrh, acute, mild and chronic, and also in catarrh of the colon and rectum. It was also used successfully in mild and chronic bronchial catarrh. Burggraeve used in it purulent bronchitis with excellent effect.

It may also be given with good effect as an antidyspeptic in torpidity of the bowels, on account of its stimulating action.

Cubebin must, however, not be used in subacute, and especially not in acute, cases before the intensity of the irritative inflammatory phenomena of the urethral mucous membrane has been mitigated; but then it can be used in high but divided doses.

Burggraeve counsels very properly to give small epicratic (alterative) doses often repeated, about sixty granules in the twenty-four hours. Laura has often given even larger doses than those in chronic urethral catarrh, with success, and without any inconvenience to the patient. Generally, however, fifty to sixty granules are enough, and at the outset one may begin with even much smaller doses pro die.

After the urethral discharge has stopped it is best to give attenuated doses during a number of days. If the object is to stimulate the stomach, it is enough to take a few granules before each meal for a few days. For catarrh of the bladder, of the bronchi, of the intestines and the rectum, we should use small doses, successively, and adapted to each case, administered according to general alkalometric principles.

As a medium daily dose we may give ten, fifteen and twenty granules a day.

Heydenreich found cubebin inert, the diuretic virtues of cubebs residing in the resin and cubebic acid, the stimulant in the volatile oil.

Felter and Lloyd give as the specific indications: Latter stage of gonorrhea after profuse discharges have ceased; chronic gonorrhea, feebleness of the rectum and large intestine; subacute inflammations of the urinary passages; urethral burning, scalding of urine in females, irritation and burning of vulva, debility with profuse mucous discharges.

CURARINE

From the Indians of the Orinoco is obtained an arrow poison known as curare. Three kinds come to the market, that which is

brought in tubes of bamboo, in calabashes, and in little clay pots. These are different in their effects and strength. Five alkaloids have been found in these, the most important being curarine.

This is a bright reddish-yellow amorphous mass, that from tube curare being quite stable, soluble in water or in alcohol.

Sollmann states that commercial curare is a most unreliable drug. Curarine causes paralysis of the nerve ends in striped muscle, followed by paralysis of nerve ends around sympathetic ganglia; very large doses depressing muscular irritability directly, and under special conditions a strychnine effect develops. Fatal doses kill by asphyxia. If not too profound the respiratory paralysis is removed by physostigmine.

Curarine given in large doses hypodermically, paralyzes the striated muscles, beginning with the short ones, the ears, toes and neck, then those of the extremities and finally the respiratory apparatus which gradually comes to a stop. The heart continues beating a while longer and then also stops. Small doses weaken the voluntary muscles alone, the respiration becoming labored but do not affect the heart.

The rationale of this action is disputed, though it evidently takes place through the blood. The ends of the motor nerves are paralyzed, but neither the trunks nor the centers. The metabolism as represented by the exchange of gases is markedly lessened, from the muscular relaxation. To this is also due the fall in temperature.

The earlier experiments with curare are inaccurate from the varying nature of the specimens, but Tillie employed pure curarine and his results are of value. He found that small doses abolish the posterior reflexes, by cerebral inhibition. Large doses affect the spinal cord directly, increasing irritability and causing convulsions, increasing to tetanic severity. This only follows the direct application of the drug to the cord.

When curare slows the heart, reduces the arterial pressure and arrests the heart in diastole, it is due to another alkaloid, curine, not to curarine. To which principle is to be ascribed the lachrymation, polyuria and salivation following some curares, is uncertain. The skin is at first dry, followed by an outburst of perspiration, dryness of the mouth and burning thirst. The temperature rises nearly two degrees.

Chattering teeth, shivering and trembling precede the pareses.

Taken by the mouth, curarine has little if any effect, even in very large doses. Either it is destroyed by the gastric juice or the absorption does not more than keep pace with the elimination.

Curarine has been employed in affections characterized by excessive irritability of the motor terminal nerves, such as tetanus and hydrophobia. Two cases of the latter have been reported as cured by this remedy. The great difficulty in obtaining it in purity, and the variable effects manifested by the curares sent to market, have prevented its general employment in affections of such gravity. Cushny considers curare not indicated in these maladies, which depend on centric irritations, while the drug acts only on the nerve-ends. But Murrell speaks highly of the use of methyl-iodine-strychnine, whose effects are identical with those of curarine, and which may be prepared in uniform strength and purity sufficient to justify its employment. In paralysis agitans, chorea, and a number of similar maladies this agent should prove of decided value.

Curarine seems to be excreted unchanged by the kidneys. It has been given in epilepsy with asserted advantage. The dose to begin with is gr. 1-250, hypodermically, increasing till effect. In hydrophobia Offenberg gave gr. 1-2 to a woman and saved her. In strychnine poisoning curare has been used with success. Here it seems to be a rational antidote. In tetanus Hoffman gave curarine gr. 1-67, increasing to 9-67, hypodermically. A case of tetany is reported in which doses of gr. 7-67 proved effective.

Curarine may be administered by the rectum, in doses somewhat larger than by hypodermic.

CYPRIPEDIN

Standard granule—gr. 1-12, Gm. .005.

Cypripedin is a concentration from Cypripedium pubescens, the ladies' slipper. No active principle has been found in this plant.

Scudder terms cypripedium tonic, stimulant, diaphoretic and antispasmodic. Its chief value is as a nerve stimulant in atonic cases, improving the circulation and nutrition of the nerve centers. Felter and Lloyd enumerate as its uses, allaying nervous excitability or irritation unconnected with organic lesions, lessening pain, producing a calm and cheerful state of mind and thus favoring sleep; hysteria, chorea, nervous headache, wakefulness, prostration in low fevers, epilepsy, all morbid irritabilities of the nervous system from non-organic causes; nervousness, hypochondria and mental depression of deranged digestion, especially in females; joint pains following scarlet fever.

Specific Indications.—Insomnia, nervous irritability, neuralgia, delirium, all from atony; menstrual irregularities with des-

pondency; tendency to dementia at climacteric; mental depression from self-abuse.

Ellingwood says the virtues of this plant are lost by drying, and only fresh root preparations should be employed. Large doses are requisite. He advises it in nervous conditions from genitourinary disorders; mental depression from sexual causes; cerebral irritation from teething; typhoid vigilance and jactitation with vital depression, and similar symptoms from dyspepsia.

These quotations show the place of cypripedin to be close to that formerly filled by valerian. Neither is a powerful remedy, but for them there is a large class of cases that do not require a very strong remedy. It is the little ailments that wear out the endurance, as bankruptcy is more easily borne than the continual nagging of a nervous, fretful wife. Cypripedin relieves the minor ailments that cause nervousness, and leaves a sense of comfort and well-being, somewhat resembling the euphoria of morphine. Possibly cypripedin may prove of value in treating the withdrawal symptoms of this and other habit drugs.

The writer has employed cypripedin largely and with satisfactory results to relieve sexual erethism. It soothes the sexual organs and quiets the irritability that leads to the exhaustion of the forces by constant discharges of energy. The patient must be warned that the effect will be a lessening of sexual desire, or else he will think it is depriving him of his powers. Explain that the energy is simply stored up by cypripedin instead of being uselessly discharged, and he will be satisfied. This result has followed the use of cypripedin in both sexes.

The dose most effective has been a grain four times a day, and the drug should be continued for a month. It is often wise to give cypripedin for a month and then follow with cornin for a similar period.

Cypripedin is one of the remedies lost to the old therapist by the uselessness of the preparations in the shops. While a freshly-made infusion probably excels, the writer has found cypripedin quite active.

DELPHININE

Standard granule—gr. 1-250, Gm. 0.00025.

The cattle ranges of the West could furnish an inexhaustible supply of larkspur, were there any demand for it. There it is a nuisance, frequently causing the death of the cattle that browse upon the young stalks in the spring. Has it any value? If it has,

way should not some good American citizens make a decent living collecting it?

We are all too apt to follow in the ruts in which we begin. We use the ancient forms of medicine bequeathed to us from the centuries, simply because we first learn them and later find it irksome to change. But if there is really a value to be obtained from this or any other wild native plant, we believe it is in a sense a patriotic duty to use it instead of relying upon remedies that come to us with a foreign stamp. We have, therefore, made some investigations of the literature of delphinine, the principal alkaloid of the larkspurs, and the results we present you. It seems to us that there are values in this alkaloid not to be obtained from any other remedy. It is not a panacea, not a remedy for any single disease; but when stripped of its encumbrances and presented in a state of purity, it seems capable of meeting certain indications as clear cut and distinct as those so beautifully met by arbutin. Like the latter, delphinine seems to be comparatively useless until it is so separated from the other principles which in the plant smother it and render it unavailing.

Delphinine is the principal alkaloid of the stavesacre or *Delphinium staphisagria*, an annual herb reaching two to three feet in height, growing abundantly along the Mediterranean coast in the south of Europe. It has alternate leaves growing on long hairy stems, palmately veined and divided into five to nine segments. The flowers are a bluish-gray, mounted on terminal stalks in the axils of leafy bracts. The part of the plant employed is the seed. The word staphisagria is derived from the Greek words, *staphis*, a bunch of grapes, and *agria*, wild. The plant belongs to the natural order, Ranunculaceæ.

The seeds of the stavesacre contain a number of alkaloids, the most important being delphinine; others are delphisine, delphinoidine and staphisagrine. These were first extracted and studied together under the name of delphinine by Lassaigne and Feneulle in France, and Brandes in Germany, in 1819. This mixture was used in all the early experiments and the true alkaloid was not separated until 1877 when it was discovered by Marquis and Dragendorff, who were able to extract a white, crystallizable alkaloid, smelling like amber and having a bitter, tingling, burning taste. Delphinine is very slightly soluble in water but dissolves readily in alcohol, ether and chloroform. (Alcohol dissolves 4.82 percent, ether 8.98 percent and chloroform 6.88 percent.) The chemical formula usually given for it is $C_{22}H_{35}NO_6$, but Brühl in his more modern work gives it as $C_{31}H_{49}NO_7$.

Delphisine and delphinoidine are similar in action to delphinine but less active; staphisagrine, however, seems to have an action more analogous to that of curare and it is probable that the difference in early experiments with impure delphinine was due to the varying quantities of this substance in the different samples of the drug employed.

Physiological Action.—During the first half of the nineteenth century many experiments were made with delphinine and the literature concerning it is surprisingly rich. But for the last two or three decades the remedy seems to have fallen into almost complete oblivion. A study of it reveals undoubted possibilities for this remedy in therapeutics. One of the first to give it attention was Turnbull of London, who in his work, published in 1835 (On the Medical Properties of the Natural Order Ranunculaceæ, etc.) gave it a great deal of careful study. Subeiran (1837), Falk and Rohrig (1851), van Praag (1854), Dorn (1857), Darbel (1864), Cayrode (1869), Weyland (1869), Rabuteau (1874), Serck (1874), and Böhm and Serck (1875), are among the other experimenters. Their experiments were largely made upon animals, including dogs, cats, frogs, pigeons, hens, etc., and even fishes. Most of these used the mixture of the alkaloids which was employed before Dragendorff and Marquis separated pure delphinine, but according to Hahn (*Dict. Encyc. des. Sc. Med.*) their results may be considered as fairly reliable, the presence of staphisagrine in varying quantities being the only element likely to cause much confusion. Rabuteau used a mixture which was peculiarly rich in staphisagrine, and he was the only one who gave much importance to the curare-like action sometimes noted.

Digestive Tract.—When taken by the mouth delphinine causes a tingling and burning sensation of the buccopharyngeal mucosa, but no profound inflammatory lesion results. The secretion of the muciparous glands is increased and there is great salivation (according to Dorn, exceeding that produced by mercurials); saliva dribbles from the mouth, the animal licks its muzzle and rubs it on the ground or other objects, probably on account of the tingling pain resulting from the local action. This phenomenon, as shown by Schroff, occurs also in veratrine poisoning. Taken into the stomach delphinine produces severe nausea, gagging and vomiting; the last may come on so early, especially in dogs, as to prevent the systemic action. To prevent this Orfila (*Traité de Toxicologie*) ligated the esophagus; other experimenters introduced the drug by the rectum. Whatever the route of administration the gastro-

intestinal symptoms were manifested. In addition there is diarrhea, and this may precede the salivation when the remedy is administered by the rectum.

Respiratory Apparatus.—More or less disturbance of respiration occurs soon after the administration of the remedy. If the dose is not too large the respiration is slowed without a preceding stage of excitement. The dyspnea which results is especially characterized by short and deep inspiration and prolonged expiration, and stertor. Serck called attention to a marked pause between inspiration and expiration and ascribed the slowing to this. *Death results from asphyxia.* When the dose is very large the slowing may be preceded by a short stage of respiratory excitement. One of the most marked actions of delphinine is its depression of respiration.

Circulatory Apparatus.—Upon poisoning with delphinine the heart is slowed and the blood pressure lowered, and finally the heart is arrested in diastole. This arrest comes a little later than the respiratory arrest. The heart in frogs continues to beat for several minutes after breathing has stopped and it is still capable of excitation for several hours after death. Life may be prolonged by artificial respiration. (Van Praag, Dorn, Weyland and Böhm.)

Urinary Apparatus.—Turnbull gave great prominence to the diuretic properties of this remedy, and it has been tried for dropsies on this account; but later investigators express doubt on this point. Van Praag says that it causes renal congestion and abundant diuresis. That it has a congestive action I can verify in my own experience, for in one case I obtained symptoms of strangury from a large dose, closely analogous to those produced by cantharidin.

Nervous System.—Early symptoms of poisoning by delphinine are, great excitement, agitation and vertigo. The animal has a staggering gait and endeavors to support itself on objects. It rolls on the ground in a peculiar manner, raising itself and then letting itself fall. Voluntary movements gradually lose their energy and precision. The paralysis of sensibility and of reflex action is more marked than of voluntary motion according to van Praag and Cayrode. In other words there is developed an anesthesia and abolition of reflex excitability; and this is shown first and most markedly in the lower extremities and trunk, less in the upper extremities and practically not at all in the head. While the skin is insensible, voluntary motion is retained. Finally complete loss of sensation and paralysis, with involuntary evacuations

occur, and the end usually comes with convulsions. The convulsions are at first clonic and finally tonic. The organs of sense retain their acuity though the pupils may be slightly dilated. A fibrillary tremor of the muscles of the abdomen may be observed; the same phenomenon has been noticed in aconitine poisoning. Serck has seen symptoms of strychnine poisoning disappear under injections of delphinine, though strychnine will not restore parts paralyzed by delphinine.

Skin.—Delphinine when applied locally produces hyperemia, itching, often a veritable inflammation and swelling similar to that produced by a mild vesicatory.

Autopsy.—The blood is dark and a little thickened, similar to that found in cholera poisoning. Passive congestion of brain, meninges, heart, kidneys, lungs, orbits; no inflammatory phenomena; heart arrested in diastole; ecchymoses in colon and rectum.

Mode of Action.—Delphinine undoubtedly exerts its action through the central nervous system—the spinal cord and medulla oblongata. The cerebrum does not seem to be attacked. Serck has apparently shown that its effect upon respiration is produced upon the center of the pneumogastric; thus, in a dog poisoned by delphinine, cutting the pneumogastric relieves the dyspnea; if the nerve is cut before delphinine is administered, then there is no slowing of respiration and it may be accelerated. Even the gastrointestinal action may be central, since the vomiting occurs whatever the route of administration; however, it may be that the drug is eliminated by the gastrointestinal route—we have no data on this point, and it is possible that the irritant action may be direct.

Delphinine shows a certain resemblance to three other drugs: veratrine, aconitine and curare. Schroff emphasized the analogy between delphinine and veratrine, calling especial attention to the nausea, the salivation and the slowing of the heart. Cayrode compares it with aconitine and says: "Like the latter (aconitine) delphinine abolishes reflex movements and allows voluntary movements to persist, but aconitine has an action more direct on the respiration and heart." The local action of delphinine resembles somewhat that of aconitine, though one writer describes the sensation produced by delphinine as more of a burning and stinging, somewhat like that produced by a blister, while that of aconitine is more prickling, like that of a mild electric shock. Rabuteau calls attention to the resemblance to curare, but this was doubtless due largely to the presence of staphisagrine. As Wayland points out, the muscular paralysis produced by curare is a peripheral action,

that of delphinine central. The *loss of the excito-motor power of the cord* seems to be the prominent feature of the action of this remedy.

Therapeutic Uses.—In recent years staphisagria has almost ceased to be used. About the only purpose for which it seems to be employed by the regular members of the profession, judging by textbook reports, is as a local application of the powdered seeds or an infusion to destroy head lice. The eclectics find it useful in a considerable variety of diseases, especially of the renal and reproductive organs, such as chronic gonorrhea, amenorrhea, leucorrhea, prostatorrhea, urinal incontinence, catarrh of the bladder, chronic irritability of the bladder, prolapsus uteri, menstrual disorders, etc. Its diuretic quality, so highly praised by Turnbull, may explain its beneficent action in these diseases. It is contraindicated in acute inflammations of the genitourinary tract, its congestive action tending to strangury and exaggeration of the local trouble.

Delphinine undoubtedly exerts an action, both general and local, presenting striking analogies to both veratrine and aconitine. In the good results to be obtained from this remedy Brühl says that he can see no essential difference from aconitine and veratrine, but there undoubtedly is a difference. As a febrifuge and circulatory depressant in acute pulmonary affections it is undoubtedly inferior to both of these, because of its peculiarly depressant action on the respiration. But in mild febriculæ its probably milder action on the circulation would suggest its more extended use, especially if cardiac weakness is prominent. This point should be worked out by trial.

Delphinine, on account of its diminution of reflex irritability and abolition of local sensibility, has a special field in neuralgias and painful affections of the nerves, also in various convulsive conditions. Turnbull suggested its use in neuralgias of the head and face, in which he used it mainly by local applications. But the fact that its abolition of sensation makes itself most powerfully felt upon the lower extremities would suggest that it could be used to good advantage in sciatica and other painful conditions of the lower extremities; while in neuralgias of the face aconitine would have a peculiarly selective action. It might be used either locally or internally.

It is worthy of a trial in convulsive conditions dependent upon irritability of the spinal cord; thus already it has been shown to be useful in strychnine poisoning, and its use is suggested in choreas,

tetanus and epilepsy. The eclectics use it in hysteria and this would seem to be justified.

This remedy has also been suggested in various affections of the eyes, such as recent amaurosis, iritis, corneal opacity, capsular cataract; also in otitis and otorrhea.

Toxicology.—According to Reil (*Materia Med. der Rein. Chem. Pflanzenstoffe*) the antidotes are tannic acid, coffee and potassium iodide.

Dosage.—According to van Praag the dose for internal use is gr. 1-8 to 1-4 three or four times daily, but it may be well to commence with a smaller dose. Turnbull used 1-2 grain at a dose, but he experimented with the old mixture. Externally gr. 1 to 4 of delphinine may be used in one dram of alcohol or lard. Merck, however, gives the commencing dose as gr. 1-67, and this is large enough for trial. As the alkaloid is rapildy absorbed it may be repeated every hour until slight irritation of the bladder denotes the beginning of toxic action, beyond which it is unnecessary to push the remedy. After that a slightly smaller daily dose may be continued as long as is deemed necessary.

The writer would especially urge a trial of delphinine in chorea and in epilepsy. Here is a field where better remedies are needed, and this would seem to be indicated on rational grounds. In the leaky bladders of elderly persons of both sexes also, delphinine should prove curative.

DIASTASE

Standard granule—gr. 1-6, Gm. .01.

This substance is an enzyme, a name used in organic chemistry to designate unformed ferments as distinguished from organized ferments.

Diastase is obtained from barley and other cereals when in process of germination. It is a saccharifying or amylolytic ferment, which has the power of slowly converting starch into grape sugar, with the intermediate body maltose. To the saccharifying enzymes belong this body, diastase, ptyalin, and the diastasic ferments of the pancreas, liver, blood, mucosa of the trachea and gall-bladder, spleen, skin, kidneys, testicles, lungs, lymphatic glands and muscles.

In the vegetable kingdom these saccharifying enzymes are very abundant, as in the buds of leaves and in germinating seeds; especially of the cereals and legumes. There is also an enzyme derived from the bacterial fungus of rice, Aspergillus eurotium oryzae, called Taka diastase, after its Japanese discoverer, Takamine.

Diastase may be found in small quantities in malt extracts, when care is taken not to disperse this substance by the heat employed in making the extract. Whether the animal diastases are identical with those of vegetable origin is yet a question. But assuming that ptyalin, the diastasic enzyme of the saliva, is at least very nearly identical with vegetable diastase, and remembering too that omnivora and carnivora produce ptyalin but very little or not at all, while herbivora produce it abundantly in their saliva, we come to the reasonable conclusion that diastase must be useful in amylaceous indigestion; and so it is found in practice.

Cushny doubts the existence of such an indigestion. He says: "Taka-diastase, which digests over 100 times its weight of starch, has been recommended in cases in which there is supposed to be a deficient digestion of starch. It ceases to act in the gastric juice as soon as the acidity exceeds 0.1 percent, but may be able to digest a certain amount of starch in the mouth and stomach before it is destroyed. The question at once arises, however, whether the ordinary digestive juices are ever unable to digest the starch of the food. And although a new term, amylaceous dyspepsia, has been introduced to indicate this class of cases, if they should be found to exist, it must be admitted that no satisfactory evidence of their existence has been brought forward as yet. It is stated that more starch is found to be digested in the stomach after the administration of diastase, but this seems to be beside the point, for it merely indicates that less starch reaches the intestine for the pancreatic juice to act upon. Until it is shown that in some cases the digestion of starch by the intestinal ferments is insufficiently performed, the diastase preparations would seem to be superfluous. According to Friedenwald diastase increases the digestion of starch in the stomach chiefly in cases of hyperacidity; but doubt is thrown upon this statement by the investigator."

Practice, however, does not sustain this skepticism. We do meet with cases where starchy food is badly digested and eructations of odorless gas follow its ingestion, in which diastase serves an excellent purpose. Moreover, diastase hastens the natural amylolytic or saccharifying process. The usefulness of diastase in diabetes mellitus, especially from pancreatic disturbances, when the withholding of bread becomes intolerable and it must be allowed to some extent, rests upon this hastening quality. What exhausts the patient here is the protracted process of the saccharification of starch. It seems, therefore, that when this process is quickly performed and the sugar gotten rid of by the excretions, this

is the cause of the patient's comparative relief, and this gives him a better chance to improve under other appropriate treatment.

Diastase is an albuminous body, obtained by precipitation from a watery malt extract, as a white powder. The minimum dose is gr. 2, and reasonably more when indicated.

As with the other artificial digestants, the effects of a few grains of diastase are immensely greater than those attributable to its own digestive powers. The function of these bodies seems to be to set the digestive process going. The secretion of the natural digestants elaborated in the body appears to be regulated automatically, and ceases when enough has been provided for the need. But sometimes the secretion is not begun, and food may be vomited hours after its ingestion, without any sign of digestive action. Now if the digestion is begun by artificial agents, it seems that the process once set in operation is continued by the forces of the digestive system, until completed. This explanation is in harmony with the facts observed clinically.

Diastase acts only upon the carbohydrates, and only during the alkaline period of digestion. It should therefore be given only at the beginning of the meal, and with starchy food. As soon as the flow of gastric acid begins the action of diastase ceases, and it is exceedingly doubtful if it is resumed later in the duodenum, as the diastase is itself almost certainly digested in the stomach. Even when clearly indicated the use of diastase should not lead the physician to neglect the necessary instructions to his patient as to correct eating. If people thoroughly masticated and insalivated carbohydrates and did not wash their food down with fluids, especially iced ones, there would be little need for diastasic aids.

DIGITALIN

Standard granule—gr. 1-67, Gm. .001.

From the leaves of the foxglove, Digitalis purpurea, we obtain the greatest of the cardiac tonics. The leaves contain at least five glucosides, known as digitin, digitalin, digitalein, digitoxin and digitonin. Of these the first is admitted to be inert, the next three resemble each other in their effects as cardiac and vascular tensors and diuretics, while the fifth to a certain extent antagonizes the actions of the others. These active principles exist in the plant in varying proportions. The strongest digitalis is said to be the wild plant of England; that found in Roumania is very much less active, while the cultivated herb is inert. The plant is a perennial.

The leaves are only active within a year from the time they are gathered. Whether the irresponsible herb collector cares for such nicety, or if he collects the wild plant when it is so easy to cultivate, are questions for those who adhere to the use of galenics—the alkalometrist demands something more definite and sure.

Pure digitalin is a white amorphous powder, formula $C_{29}H_{38}O_{12}$. It dissolves with difficulty in water, easily in alcohol or chloroform. The solution is very bitter. It is precipitated by tannic acid.

Physiologic and Toxic Actions.—A lethal dose of digitalin paralyzes the heart, arresting it in diastole. The pulse is first slowed, the arterial tension increased. The pulse is then accelerated, the blood pressure falling slowly and progressively, interrupted by brief elevations. The heart-action becomes very irregular, pulse-rate variable, arterial pressure continually falling; finally, sudden heart paralysis and arrest in diastole.

Traube describes three stages: The arterial pressure rises and the pulse slows; the pulse-rate rises suddenly to its maximum, as in atropine poisoning, the arterial pressure rising at the same time, but soon beginning to sink gradually to below normal; the pressure still sinks, the pulse again slowing, intermitting and irregular, the beats weaker, finally stopping in diastole.

Small doses have no appreciable effect on the nerve centers of a healthy man. They sedate the nerves and favor calm and sleep, when there is agitation and insomnia (Rabuteau).

Toxic doses, or even smaller ones too long continued, provoke vertigo, headache, obscurity of vision, dilation of pupils, ringing of the ears, hallucinations, muscular weakness, dulling of the senses and the general sensibility, sometimes convulsions. These are due to the circulatory disturbance and the increase of carbonic acid in the blood.

In small doses digitalin does not weaken the contractility of the voluntary muscles but in large doses it extinguishes it rapidly. Small doses excite the contractility of smooth muscle fiber; large doses lessen or abolish it.

During the first stage the thermometer in the anus shows a fall of temperature, while at the surface of the body the heat is augmented. This is explained by the increase of the arterial pressure, the acceleration of the cutaneous circulation, and the radiation of heat. The fall of temperature in the following stages, and in fevers, is explained by attributing to digitalin the power of removing the causes of abnormal hyperthermia, or of indirectly diminishing the

molecular changes and the production of heat, by slowing the circulation.

Small doses of digitalin produce no notable effect on the gastro-intestinal tube of a healthy person. Larger ones cause nausea, anorexia, vomiting, gastric disorder and diarrhea (Koppe).

Digitalin is not a true diuretic, and has no value as a renal eliminant, unless the defective action depends on heart-disease. In healthy persons by raising the arterial pressure to an abnormal degree it lessens or suppresses the discharge of urine. Sometimes the excretion is reestablished as the pressure falls; in others it only returns when the pressure has become subnormal. Here the renal vasomotors seem to be affected more than the general system. After these arrests the urine is always albuminous. But other elements may enter to explain the action on the excretion of urine. Increased arterial pressure may check it by mechanical action.

The slowing of the pulse in the first stage is attributed by Traube to direct excitation of the centers and peripheric intracardiac ends of the vagus. Meyer looks on the slowing as secondary to the increased vascular pressure, the intracranial tension acting on the vagus centers. This regulates automatically the discharge of blood into the cranium. But Traube found that cutting the cervical cord—which lessens arterial pressure universally—does not prevent the slowing of the pulse by digitalin. Binz does not consider these views antagonistic.

How digitalin increases the blood-pressure is no better comprehended. Binz attributes it to a direct action, since neither atropine nor section of the inhibitory nerves prevents it. Traube attributes it to excitation of the cardiac excitomotor nerves. But as on the excised heart of the frog digitalin acts precisely as on the heart of warm-blooded animals *in situ*, there seems to be a direct relation between the drug and the cardiac muscular fibers. On the contrary, Ackermann and Kaufmann consider that by acting on the vagus centers and peripheric terminals, it augments the intravascular pressure. Binz says the arterial pressure depends on three factors: Increased energy of ventricular contraction, increased frequency, greater resistance from increased systemic vascular tonicity.

The unquestioned diuretic property of digitalin in cardiac dropsies is thus explained: There is here often a serous transudation into the tissues, due to the enormous passive venous hyperemia. Digitalin regulates the abnormal distribution of the blood, removes the hyperemia, and permits reabsorption of the effused serum. The aqueous blood, and the general increase of vascular pressure, espe-

cially in the renal arteries, conduce naturally to hypersecretion of urine (Nothnagel). Gubler calls attention to the corresponding diminution of perspiration, for while the activity of the sudoriparous glands is in proportion to the peripheral congestion and exaltation of the temperature, that of the uropoietic glands is in inverse ratio to the vascular erethism.

The urinary flux requires two opposite conditions: The absence of sanguineous congestion of the kidneys, the expansibility and perfect contractility of its vascular apparatus, as well as the rapid circulation of the blood in the interior of the gland. Increase of tension becomes then an accessory circumstance. The energized cardiac contractions have more importance; they accelerate the flow of blood into the renal parenchyma, and contribute powerfully to the definite result. The diuretic action of digitalin is the more pronounced the more directly the anuria is dependent on the disorder of the circulation; and the aqueous plethora or the serosity in closed cavities or cellular tissues is the more abundant.

Sollmann says that the typic effects of digitalis are produced in the absence of nerves and are therefore purely muscular. Digitalis counteracts the effects of muscular depressants. It increases the tone of the cardiac muscle as veratrine does that of the skeletal muscle. Both stimulate cardiac, smooth and striated muscle, veratrine influencing the latter the more, while digitalis affects the others more (Bottazzi).

Gottlieb and Magnus showed that the action of digitalis on the blood-vessels is mainly peripheral, and is exerted directly on the arterial muscle. Vasoconstriction is most marked in the splanchnic area, the peripheral vessels being even dilated. Gerhardt determined that the pulmonary vessels are scarcely affected. Digitoxin powerfully constricts the coronary arteries, strophanthin does not (Loeb).

Several hours are required before the effects of digitalis are manifest, according to Sollmann. Fraenkel asserted that digitoxin required sixty hours, digitalin thirty, to develop their action. Germanic digitalin, consisting of almost pure digitalein, shows unmistakable effects within half an hour. Digitoxin is the most irritant to the stomach, the most apt to cumulate, and exerts the greatest vasoconstriction. Its effects once established are also most enduring. This applies to the tincture of digitalis in which this glucoside predominates. Digitalein has the least vasoconstrictive action of all, acts most promptly and is least likely to cumulate.

The advantages derivable from digitalis, according to Sollmann, are a slow heart, systole and diastole both lengthened, increased

strength of beat, tendency to the systolic phase, and rise of blood-pressure. The prime indication is a rapid pulse with low pressure.

Digitalin causes no local effects when introduced into the cellular tissues.

Digitonin, $C_{27}H_{46}O_{14} + 5H_2O$, was obtained by Kiliani in needles grouped into wart-like bodies. These dissolve sparingly in cold water, and do not separate from a hot solution when cooled. Its irritative effects closely resemble those of saponin.

The digitonin of Van Renterghem is a white amorphous powder, dissolving readily in water, or in alcohol, and is precipitated by tannic acid. He gives it the formula of $C_{31}H_{52}O_{17}$, as does Schmiedeberg.

The resemblance of digitonin to saponin is so close that Van Renterghem avails himself of studies of the latter, for want of accurate observations on digitonin. Hypodermic injections of saponin gr. 1 1-2 caused edema and erysipelatous inflammation at the point of entrance. Soon after there were grave headache of the right side, intense pains in the eye and the extremities, with bodily and psychic depression. The temperature fell notably and it was only after five hours of very serious indisposition that the experimenter escaped an imminent death.

Taken by the mouth, it excites cough and exaggerated secretion of the laryngeal and bronchial mucosa for many hours. Doses of gr. 1 1-2 to 3 do not cause toxic symptoms, nor do they augment the secretions of the skin and kidneys. Applied to wounds or mucous surfaces it causes lively pains and plastic exudations. Injections in animals cause paralysis of motor and sensory nerves around the site of the injections, extending towards the cord.

Carried immediately to the cord, saponin after preliminary tetanic symptoms, causes central paralysis, extending to the peripheral nerves. The action extends to the whole muscular system, striated, cardiac, and the smooth fibers of the gastrointestinal tube. Entering the circulation it exerts a triple action upon the heart; annihilating the excitability of the muscular tissue, paralyzing the peripheric fibers of the pneumogastric and the inhibitory centers, as well as the accelerator nervous fibers of the sympathetic. By this the heart-beats lose their energy, the circulatory center is paralyzed, and the heart arrested in diastole.

With warm-blooded aminals these phenomena are followed or accompanied by a fall of the vascular pressure, of the animal heat, and of the respiration.

The administration of digitalin can then prevent death. Digitonin is less energetic than saponin.

Toxiresin and digitaliresin, decomposition products, closely resemble picrotoxin in their effects. By exciting the pneumogastric and the vasomotor centers, they occasion weakening of the pulse and elevation of the arterial pressure.

Digitonin forms half the mixed glucosides from the seed, but is less abundant in the leaves. It enters into the composition of Germanic digitalin. The yield is from 4 to 5 percent.

Digitalein, $C_{22}H_{38}O_9$, forms small round granules, very soluble in water and in alcohol, insoluble in ether, chloroform or benzol.

The taste is very bitter and sharp. It is precipitated by tannic acid. Administered hypodermically, it causes no irritation.

Schmiedeberg's digitalein is a yellowish-white amorphous powder, intensely bitter. Merck gives the dose as gr. 1-64, to 1-32, two to four times a day.

Digitoxin, $C_{21}H_{32}O_7$, occurs in needles of nacre luster, insoluble in water, soluble in chloroform, or in hot alcohol. When administered hypodermically it causes phlegmonous inflammation.

The effects of a medicinal dose last 8 to 10 days. Doses of gr. 1-33 endanger life. It is not precipitated by tannic acid.

The emetocathartic effects follow its topical application as well as its administration by the stomach.

Merck gives the dose as gr. 1-250 to 1-125, three times a day, with 3 m. chloroform, 60 m. alcohol and 1 1-2 oz. water. Maximum daily dose gr. 1-32.

The yield of digitoxin is about 0.4 percent. It is very slow in developing its action, and may be precipitated in the alimentary canal and reabsorbed *en masse* later, thus throwing the whole effect on the system at once.

Nativelle's crystallized digitalin consists of one-third pure digitalin and two-thirds digitin. The "pure" digitalin is a mixture of digitalin, digitoxin and toxiresin.

Nativelle's amorphous digitalin consists of digitalein.

Homolle and Quevenne's amorphous digitalin is composed principally of digitalin, with the formula of $C_5H_8O_2$.

Digitalin Germanic of Finzelberg: A mixture of digitalin and digitalein.

Pure digitalin Germanic: This is principally digitalein.

Schmiedeberg states that digitoxin, digitalin and digitalein exert an absolutely analogous action; the differences being simply those due to their diverse solubility, and energy of action. Digitoxin is from six to ten times stronger than the others.

The cumulative action of digitalis has been much discussed. Gubler distinguishes between the accumulation of doses and that of effects. Given in pills or powders, their want of solubility or unfavorable conditions of absorption may cause an accumulation of the doses in the alimentary tube. When the conditions here favor solution and absorption, the whole collection may be poured into the blood at once.

The accumulation of action depends on the elimination, which may cause the retention of part or all the drug in the body, until enough has accumulated to cause toxic effects.

The habitual use of a remedy also entails a gradual diminution of its effects, as the impressibility of the body diminishes or the antagonistic forces increase.

The first of these difficulties, accumulation of doses, cannot be avoided as long as the physician uses galenic preparations, as he cannot tell whether he has simply given a weak dose, of old leaves perhaps, or that the dose has not been utilized. These perils are avoided by the use of the active principles. And if all the various socalled digitalins were retired but one, this would quickly be done. But since digitoxin dominates in the preparation of Nativelle, digitalin in Homolle and Quevenne's, and digitalein in the Germanic, any one of these is preferable to the crude digitalis, bearing in mind the difference in strength and solubility of the three principles mentioned.

Koppe found that two milligrams (gr. 1-33) of digitoxin, a single dose, given an adult man, caused toxic symptoms very violent and persisting many days. Megevand took one-third of a milligram (gr. 1-200) of Nativelle's digitalin once a day for six consecutive days. The pulse began to slow on the second day, fell more rapidly each day, the lowest point being reached on the seventh day, when he felt nausea followed by vomiting and headache, intense and persisting till the following day. The pulse had fallen to 48, and it was not till the twelfth day, six days after ceasing the use of the drug, that it returned to its normal rate, 67 to 70.

The insolubility of digitoxin in water furnishes a sufficient reason for discarding it.

Megevand took for seven consecutive days a daily dose of four milligrams (gr. 1-16) of Homolle and Quevenne's digitalin. On the fourth day came the first fall in the pulse, of five beats; on the sixth and fifth it fell to 55; and it was four days after the cessation of the drug that the pulse returned to its normal rate of 67. Toxic symptoms due to the accumulation of this digitalin were observed

by Homolle, as nausea, headache and delirium. These disappeared after twenty-four hours.

Chemically pure digitalin, and Homolle and Quevenne's products, are but slightly soluble in water, and present, after doses not too strong and repeated for some days, commencing intoxication. They are therefore not the best agents for use. Goerz used chemically pure digitalein; taking for ten days granules containing a milligram (gr. 1-67), beginning with one granule and adding one each day up to five. The pulse fell from 54 to 46, becoming fuller, stronger, but more irritable; that is, after slight exercise it rose to 128. He felt slight headache, anorexia, great weakness and epigastric pressure.

Van Renterghem took for fifteen days eight milligrams of digitalin Germanic (digitalein), in two equal doses. No dyspeptic symptoms or slowing of the pulse were noted. But the same preparation, given to a patient with chronic pneumonia while affected by a hemoptysis without fever, brought the pulse from 96 to 62, and stopped the bleeding. The remedy was given in water, a milligram (gr. 1-67) every half-hour.

In a case of ascites Van Renterghem obtained diuresis and cured the patient, without lessening the pulse-rate. In a galloping phthisis the use of Germanic digitalin, 20 milligrams (gr. 1-3) a day, with aconitine, veratrine, strychnine and quinine, caused on the fourteenth day aching about the eyes and anorexia; the digitalin was stopped and the veratrine doubled, when the headache and dyspeptic symptoms subsided. He gives the preference to this digitalin, as being perfectly soluble in water and presenting the least danger of cumulation.

The organism easily accustoms itself to digitalin. Given daily in moderate doses it may be continued for years without toxic effects, but produces its physiologic action on the cardiac muscle and prevents fatty degeneration.

Digitalin is eliminated in part by the kidneys (Dragendorff).

Huesemann calls attention to the danger of accumulation in cases of ascites with chronic nephritis as the renal elimininations is here defective.

Synergists.—Many agents are ranked among the cardiac tonics. Digitalin, antiarin, helleborein, euonymin, and thenetin, crystallizable glucosides; scillain, adonidin, oleandrin, non-crystallizable glucosides, little soluble in water; digitalein, nerein, apocynein, convallamarin, amorphous glucosides, very soluble in water; digitoxin, strophanthin, apocynin, not glucosides, partly crystal-

lizable; tanghinin, neriodorin, neriodorein, upas, whose nature has not yet been studied sufficiently; erythrophloeine, an alkaloid combining the effects of digitalin and of picrotoxin; phrynin, derived from some kinds of frogs, affecting the heart like digitalin and causing local irritation; caffeine, which regulates the heart, augments its energy, slows the pulse and raises the arterial pressure.

Among the auxiliaries are, as antipyretics, veratrine, aconitine, quinine; vascular tonics, arsenous acid, iron, ergotin, strychnine; as diuretics, aconitine, neutral alkaline salts, turpentine; as cerebral calmants, strychnine, aconitine, hyoscyamine, morphine.

It is usually advisable to give digitalin when indicated, up to the desirable effect; when this begins to fail, add one of the other cardiac tonics, and later another, instead of increasing the dose of digitalin.

Antagonists.—Atropine and chloral paralyze the nerve-ends of the pneumogastric in the heart, and prevent the slowing of the pulse, without affecting the increase in the arterial pressure.

Koehler says saponin antagonizes digitalin, and therefore digitonin does so also. The stoppage of the heart in systole due to digitalin is obviated by saponin, which neutralizes the excitation of the inhibitory nerves; while digitalin in turn by exciting strongly the cardiac muscle suppresses or abolishes the paralysis of saponin.

If too large a dose of digitalin has been given, the stomach should be emptied by emetics and the pump or lavage, then tannic acid given in repeated doses to render the poison insoluble; when absorbed, measures are to be taken to favor elimination, as by the use of saline purgatives and diuretics. Stimulants should be given internally—camphor especially—and rubefacients applied to the skin with rubbing, and heat applied. Coffee and tea are contraindicated.

The danger in digitalis poisoning may last for several days, during which a sudden movement or even psychic excitement may occasion sudden stoppage of the heart. Absolute quiet must therefore be enjoined, even after improvement has set in and a subjective feeling of well-being is present. Anything calculated to occasion vomiting is to be avoided, such as free drinking.

But poisoning is usually due to single large doses. The cumulative effects are limited to gastric irritation, headache and stupor; preceded by nausea, supraorbital tension, weak feelings in the epigastrium, photopsia, insomnia and tinnitus. These subside when the medicine is discontinued.

Therapeutics.—The therapeutics of digitalin is to be deduced from its action, in strengthening the heart, contracting the blood-vessels, and increasing the excretion of urine. It is of the utmost importance that the physician using this potent drug shall know exactly how to secure the greatest benefit from it; and just when the maximum has been attained. The indication of exact dosage is to be taken from the pulse, for the useful action is manifested there rather than in the heart itself. It is obvious that digitalin can add no real strength directly to a weak heart. There is no nitrogenous element in the glucoside that will act as a heart food. The benefit directly obtained from its action on the heart is therefore in the nature of stimulation—the whip that urges on the tired horse a little farther when he begins to flag. And there is this further disadvantage, that by contracting the coronary arteries the nutrition of the heart is lessened, and the supervention of fatty degeneration hastened. But if the effect of digitalin on the arteries is taken as the measure of its activity we have a very different story to tell.

Take a membranous tube like the small intestine, and try to force water through it; the force will be expended in dilating the relaxed walls of the tube, and you may increase the force until you burst the tube, and yet you cannot force the water through it. But if you take a tin tube of equal length you can with ease force the water through. There is no force expended in dilating the walls. Now if just enough digitalin is given to impart normal tone to the relaxed blood-vessels, a great obstacle will be removed from the heart, and its work will be thus made easier. By this the work the organ must do is reduced so as to come within the limits of its strength, and with this physiologic rest there will be an improvement of the heart's nutrition. In this way, and in no other, digitalin may be made curative to maladies of the heart with loss of power. And if thus given the drug may be continued for very long periods without injury, but with distinct benefit. But if the doses are increased till the vessels are abnormally contracted, the heart's work will be increased and exhaustion hastened. The nutrition of the cardiac tissues will be impaired.

The only other means by which a weak or imperfect heart may be made to perform its vital functions indefinitely, is by reducing its work to the limit of its strength; and this demands lessening the bulk of the blood by enforcing the dry diet. If the quantity of fluids taken into the body daily is less than the quantity cast out by the emunctories, the weight falls, mainly at the expense of the fluids of the body—the blood. If one pound of useless water is

taken from the blood, the heart is materially relieved in its work; and as the same quantity of nutritive material is contained in the concentrated blood, nutrition does not suffer.

From the foregoing considerations it is evident that digitalin is contraindicated in any cardiac affection in which the arterial tension is not below normal. When the tension is above normal, as in atheroma or in cirrhotic nephritis, there is danger in this drug. Fothergill warned against digitalis in aortic stenosis, and this is a wise caution when there is atrophy; but when hypertrophy has ensued and compensation is failing, we can obtain from digitalin the same benefit as in mitral affections.

Gubler considers digitalin contraindicated in aneurisms, in cerebral congestions and apoplexies. During the period of compensatory hypertrophy in valvular disease digitalin is not needed and its use would be dangerous; but when compensation begins to fail the utility of this drug is well shown. It is equally applicable to this condition of failing compensation, whether following mitral stenosis or insufficiency, or mixed forms, or in aortic insufficiency; though there it has been considered of doubtful utility. Gubler termed it useless here; while others have called attention to the danger of prolonging the diastole when the ventricle is already partly filled with the regurgitant blood. But even here, if the vessels need toning, there will be distinct benefit from digitalin, though it should be given in careful dosage. But advanced degeneration of the heart-substance as well as hypertrophy, are distinct contraindications. Rupture of the feeble heart-wall may result from the powerful contraction of the remaining muscular fibers. The effects are less marked in tricuspid cases since in adults they follow mitral disease.

The above view of the place of digitalin receives confirmation from clinical observations such as these: Van Renterghem says that the remedy is specially marvelous if the vascular tension is notably low. Traube and Fraenkel remark that the general symptoms improve under its use, even when no modification is evident in the frequency or regularity of the pulse. Binz does not consider impossible the claim that cases of fatty degeneration have been actually cured by prolonged use of digitalin and iron, even when complicated with dropsy and albuminuria. He attributes the benefit to the improvement of cardiac nutrition, comparing the effects on the heart with those of exercise, electricity and massage on the general muscular system.

Leyden advised digitalin in maladies of the right heart without valvular imperfections but with weakness.

Huesemann says that in paralysis of the left heart digitalin can arrest at the outset the pulmonary œdema.

In strictly functional disorders it is necessary to associate other remedies with digitalin, or to substitute cactin.

Binz thus summarizes the indications for digitalin in cardiac maladies: Pulse agitated, palpitant; stases in the lesser circulation, causing oppression, bronchial catarrh, cardiac asthma; arteries small and empty, veins overfull, skin cyanotic, sensation of cold, nutrition impaired, serous transudations in the subcutaneous tissues of the lower extremities and in the peritoneum; urine secretion much diminished.

The second use of digitalin is as a remedy in fevers and inflammations.

With aconitine it forms the basis of the alkalometric treatment of fever, their use being based on the following reasoning: The first stage of any inflammation is hyperemia, the presence in the affected tissues of an abnormal amount of blood. There is not an immediate increase in the body's supply of blood, but an abnormal distribution of that previously existing. It follows therefore that the presence of too much blood in one part necessitates the admission that there is too little blood somewhere else. The excess of blood is at first to be found in the vessels, and the capillaries are dilated and engorged. But this must mean that the vasomotor nerves governing the caliber of these vessels are paretic, else they would not permit the entrance of too much blood, and the dilation. And as the vessels elsewhere have too little blood, they must be in a spastic state, being unduly contracted. Hence, for every vasomotor paresis in an inflamed area there is a vasomotor spasm elsewhere; and these two conditions exactly balance each other. The beginnings of an inflammation may be opposed either by stimulating the paretic vasomotors to contraction, or by relaxing the spastic vasomotors to allow the blood to flow back into the contracted vessels in normal quantity. All direct treatment of fevers is based on one or the other of these two therapeutic principles, and the history of medicine shows a constant oscillation between them—as was once said, "we bleed down to the brandy point, and then brandy up to the bleeding point."

It remained for Burggraeve to demonstrate the previously unsuspected fact, that both these processes could be induced in the same body at the same time; and that the paretic cells would take up the needed doses of stimulants, and the spastic cells what they needed of sedative agents, as each cell in the body takes from the

common supply of blood just what food it requires and passes the rest by. Hence, there is no real antagonism between such tensors as digitalin and relaxants as aconitine, but when they are administered at the same time each does its work where it is needed. Taking these as the basis, we find that some cases show an abnormal weakness of the heart and of the general vitality; and this induced Burggraeve to add the powerful vital incitant strychnine arsenate, making a triad whose efficiency in all asthenic types of fever leaves little to be desired. And as many cases show an excited, overacting heart, and a deficiency in the elimination of toxins from the body, Abbott was inspired to add that great sedative and unlocker of elimination veratrine, making a second triad for the sthenic forms of inflammation.

On these two combinations is based the alkalometric treatment of fevers. By their use the temperature is held within safe limits, the excessive expenditure of vital force is checked, the excretion of waste and imperfectly elaborated products is facilitated, which if retained in the body would increase the fever; while nutrition is favored, inanition prevented, and the patient is put in a state to better resist the onslaughts of disease.

The writer believes this method compares favorably in intelligibility and is far superior in results over the ordinary methods of veering aimlessly between alcohol, quinine, coal tars, strychnine, digitalis, baths, and the procession of sedatives and stimulants that succeed each other kaleidoscopically.

The gentle but persistent action of these alkaloids, an action exerted upon the innate causes of the derangement instead of simply smothering the symptoms of their effects, commends itself to any physician who will sit down and observe what follows their administration.

Liebermeister found digitalis useless or even injurious during the febrile period, but when the fever had fallen and the pulse still remained fast, this agent acted admirably, in moderating the cardiac movements. Binz says that as an antipyretic digitalis can do no good when in fever the blood-pressure is normal or above normal; but if it is below normal at the time of the administration of this drug it will show the same benefits as in the corresponding state when due to heart-disease. Van Renterghem calls attention to its action as a sedative to the vascular erethism. By contracting the vessels it lessens oxygenation in the tissues, and thus prevents heat production. The principal indications for digitalin are found in acute pneumonias, pleurisies, endo- and pericardites; where it

lowers fever, frees the pulmonary circulation and limits the spread of the inflammation. Associated with the remedies mentioned, it is of real service in typhoid fever, the eruptive fevers, acute continued fevers and hectic. It is of value also in acute ocular inflammations, cystitis, rheumatism; in a word, in all maladies characterized by a rise in temperature, digitalin and its associates are of premier importance.

To estimate properly the effects of digitalin as a diuretic we must remember three influences that are exerted on the excretion of urine: The renal circulation, the composition of the blood, and the nervous influence. Digitalin acts principally by modifying the renal circulation. It is in passive renal congestions accompanying organic heart-diseases and in blood stases from functional circulatory affections that it finds its field. The general acceleration of the circulation enables the renal veins to better discharge their contents. Gubler says renal congestions are found in simple nephrites, those dependent on diatheses, such as gout, uricacidemia, in the decline of fevers, and analogous cases. Digitalin is diuretic by increasing the renal vascular pressure, not by stimulating the excretory apparatus. It is useless in hepatic dropsies, the cancerous cachexia, etc. The dialysis-stimulants, the saline diuretics, aid the action of digitalin.

Digitalin has a certain influence in calming excited states of the brain. Mason Cox valued it very highly in mania. I have succeeded by its use in quieting noisy maniacs when all other means failed. Fothergill advised this remedy especially in the mania of drunkards, where it relieves the cerebral anemia. Huss and Gunsburg recommended it in delirium tremens, where it replaced opiates some years ago. The tincture was given in doses up to two ounces. Certainly digitalis is preferable to opium, but the eliminants have replaced both. Nevertheless there are cases in which this remedy is indicated and very beneficial. The weak and rapid heart calling for it is sometimes seen in these subjects.

Huesemann advised digitalin in delirium with inflammation and fever; such as the pneumonias of drunkards. But Gubler attributed the benefit to its effect on the hyperemia or the fever present. And as in epilepsy the crisis is always accompanied by an afflux of blood to the nerve centers, we can with benefit direct against it digitalin, as we do other remedies such as the bromides.

Burggraeve recommended to oppose to the delirium of drunkards, always asthenic, digitalin, aconitine and strychnine; stimulating the heart, vasomotors and nerve centers

As a remedy for hemorrhages, digitalin is too slow for emergencies; but the writer has had this curious experience: In a number of postpartum hemorrhages, he has given ergot until the flow was reduced to a small one—mere oozing—and beyond this ergot would not go, no matter how large the doses. Then if digitalin were given, the remaining hemorrhage was stopped entirely.

The constant appearance of articles dealing with the preparations of digitalis shows the importance of the remedy, and the failure of the profession to fix upon any one form as satisfactory. France and Italy have long since settled upon digitalin as their chosen heart tonic, and for many years the topic has scarcely been discussed there. Forty years' demonstrations of the value of this principle, which affords all the advantages and none of the disadvantages of digitalis, seem to have taken the question out of the realm of debate. Unfortunately, in America the question appears to have become involved with that of the commercial interests of the houses that produce the various foxglove preparations.

Laura says: "I hope that digitalis in substance and its official preparations may be soon banished from therapeutics forever. I believe that it is necessary under all circumstances to give pure digitalin the preference over the doubtful and dangerous digitalis. This fact is founded so logically and so clearly on the demonstrations of science that it imposes itself henceforth upon every physician as an imperious duty."

Writers are not in accord as to the best time to collect the leaves of digitalis. Schneider places the proper time in August and September; Hepp only asks that they be collected from plants of the second year's growth, a little before flowering; others say the best time is during the florescence. But the yield of active principles varies as the florescence advances.

Jaccoud, a partisan of crude digitalis, said: "Do not slumber in a false security; whether you prescribe a single large dose or prolong beyond measure the use of full doses, you pass suddenly from the therapeutic to the toxic action; and see what occurs—with or without gastrointestinal phenomena, with or without cerebral accidents, the heart weakens, takes on an unusual frequency, the pulse becomes rapid, small and compressible, the phenomena of venous stasis appear, the face becomes cyanotic, in one word, you have an artificial asystolia that, if it is prolonged, will kill your patient as surely as a spontaneous asystolia."

This had been demonstrated experimentally as early as 1856 by Traube.

Speaking of the applications of pure digitalin Laura says that it is always necessary when the heart is enfeebled in its forces, irregular in its rhythm. The life of this organ is of even more importance than its material condition. Digitalin is *par excellence* the special therapeutic modifier, one could almost say the vital medicament of the heart."

Hatcher said that the strength of digitalis prepared in July varied by 400 percent from that prepared in September.

Dosage.—The subcutaneous method is not suited to digitalin, because even using the soluble digitalein it occasions some irritation, and because a remedy demanding such nicety as to dosage requires too many punctures when thus employed. To control hemorrhages, to combat depression resulting from snake bites or mushroom poisoning, digitalin may be thus given as an adjuvant to or substitute for strychnine or atropine.

Merck gives the dose of digitalin "German" as gr. 1-64 to 1-32, four times a day; maximum daily dose gr. 1-3.

Van Renterghem advises for infants two years old a granule, gr. 1-67, every half-hour; for older patients, two or three granules thus repeated. Especially should the remedy be watched when given to a patient for the first time, and in nephritis. Renal impermeability is a contraindication, as it is of so many other remedies. The space of a half-hour between doses allows enough time for absorption; less than this would not.

How soon does digitalis show its effects? Traube says, in twenty-four to forty-six hours; Rabuteau puts the time at ten to twelve hours for the digitalin of Homolle and Quevenne; while Van Renterghem claims that the Germanic digitalin displays its physiologic effect in four to six hours.

Huchard commends three ways of giving digitalin in cardiac affections. The first is to give 1-20 grain in one or two doses for one day. In from thirty-six to forty-eight hours abundant diuresis sets in. If not sufficient this is repeated in eight to ten days. When diuresis ceases very small doses should be prescribed after a fortnight and continued for three or four weeks. In the second, sedative or weak doses are given. Palpitation and dyspnea are relieved in mitral diseases, even during perfect compensation. From 1-200 to 1-100 of a grain is given for five consecutive days and repeated every three or four weeks. The third is the cardio-tonic dose, which exercises a cardiac but not a diuretic action, and should be continued for weeks and months with intervals of rest from time to time. From 1-300 to 1-250 of a grain once a day suffices.

M. G. Price says: "When digitalis seems inert, if given by the mouth, there may be rapid improvement following the hypodermic injection of digitalin. When digitalin is contraindicated by bad action or nausea and vomiting, convallamarin is better, and this is also a diuretic."

I have frequently noted the effect of the water-soluble digitalin unmistakably manifest within half an hour of its administration by the stomach.

If gastric irritation is manifested the remedy should be suspended until all such symptoms have disappeared. As soon as the pulse slows, lessen the frequency of the doses, and stop altogether if the fall continues or when the rate approaches the normal. In a young and healthy man this is about 66 when lying down, 71 when sitting and 81 when standing.

How long may digitalin be given with benefit? I have administered the Germanic digitalin (digitalein) to patients with organic affections of the heart, in doses of gr. 1-4 thrice a day, for years, without harm or wearing out of the remedy.

Some years ago Henry Beates, of Philadelphia, published a remarkable paper in which he called attention to the superiority of Germanic digitalin over all the other preparations of digitalis, his conclusions being that this substance is a derivative not contaminated with other active principles, possessing uniform and unvarying strength, relatively free from that property which produces gastric irritation, a powerful stimulant to the whole cardiac apparatus, and a reliable and pronounced stimulant to the vasomotor system, which does not develop cumulative action, the adult dose ranging from 1-10 of a grain as a minimum to 1-2 grain as a maximum. He found it applicable to all lesions of the heart, with the single exception of mitral regurgitation complicated by dilation of the auricle.

Ten years later, Dr. Beates stated that his further clinical experiences have more conclusively proven the therapeutic value of this digitalin. During these ten years he has treated numerous cases with this product, in the doses and manner outlined, with the most satisfactory results. He says: "I cannot too strongly urge upon physicians the liberal use of digitalin in cases with circulatory disturbances. In collapse of pneumonia, in typhoid fever and in surgical shock as large as two-grain doses in 25 cubic centimeters of salt solution, hypodermically, have been successfully employed in several instances." Dr. Beates, as the head of the Pennsylvania State Examining Board for many years, is a man of unquestionable standing; more than that, in his ability as a clinical observer he

has few rivals and no superiors, even in that center of medical culture, Philadelphia. Such testimony is of infinitely greater value than that of any number of even the most accomplished pharmacists.

Reynolds Webb Wilcox said that the indications for the use of digitalis were laid down as long ago as 1783 by Withering. It is indicated, as a rule, when the heart-action is rapid and feeble and the arterial tension low, and contraindicated when the heart-action is strong and the arterial tension high. It has some marked defects, the principal one of these being the vasoconstriction which it produces. On this account strophanthus is suggested as a substitute in similar cases. It is less of a vasoconstrictor than digitalis, and has a more rapid action. Dr. Wilcox thinks that it should be used instead of digitalis in cases of children and the aged. Convallaria is found untrustworthy, and adrenalin he considers objectionable on account of the renal irritation which it causes. Erythrophleum, or sassy-bark, is another cardiant of which he has made a careful study. He finds it more active in slowing the pulse and more desirable as a vasoconstrictor than digitalis; in fact more than digitalis and ergot combined, but it is irritating to the stomach. On the whole, while less cumulative than digitalin, it is also less reliable. He thinks that its use should be confined to those cases of fairly competent heart with low vascular tension, in which it would show its effect more rapidly and markedly, and in those cases in which digitalis had lost its usefulness or had entirely failed to secure the expected action.

"There is only one drug," said the speaker, "which increases both the force and frequency of the pulse, and that is cactus. It is especially useful in neurotic heart and slow heart. If an active preparation is used, and such is readily found in the shops, brilliant results are obtained in appropriate cases. In pulmonary edema with heart-failure I do not know of any remedy as good as hot coffee given by high rectal injection. By combining with each dose half a grain of caffeine sodiobenzoate we could get along with much less digitalis than otherwise. Strychnine is sometimes of service in cardiac disease, but one difficulty with it is that patients readily become habituated to its use."

One of the nice applications of this active principle is in the relief of insomnia dependent on vasomotor relaxation. The vascular tone being deficient, the patient while erect is somnolent from cerebral anemia, the feeble heart being unable to sustain the column of blood and raise it to the head. On lying down the blood flows to the brain, where the relaxed vessels are not strong enough to

resist the force of gravity, and the cerebral anemia necessary for sleep is wanting. A physiologic dose of digitalin exactly relieves this condition, and secures a healthful sleep.

Some observers have advised that a single dose be given and only repeated at very long intervals—one says six weeks. The idea is that as given to compensate for the leakage of the valves, we should wait until there has been an accumulation of surplus blood in the ventricle. But this is obviously *a priori* reasoning; and as a leakage of a single drop would in an hour reach the quantity of nearly half a pint, there is a fallacy present. If the mechanical theory involved in the "dry diet" be adopted, it will be found that the doses of digitalin may be gradually diminished, as less will be needed to maintain the circulation.

Liebreich mentions as an indication for stopping digitalis the occurrence of a pulse in pairs, with a longer interval after each two beats. Paroxysmal tachycardia also seems a contraindication. The dilation is apt to indicate disease of the heart-walls and digitalin may then do great harm. It is specially dangerous with fetal pulse.

In exophthalmic goiter digitalis does well, if given carefully. In dropsies with emphysema digitalin is not to be used as long as hypertrophy of the heart endures.

The cardiac indication in exophthalmic goiter varies with the phases of the disease. In the early stages while the heart is hypertrophied the vascular relaxants, veratrine and aconitine are needed and give relief. As hypertrophy reaches its limit and the circulation begins to fail, we find place for digitalin and strophanthin. Given too early cardiac tensors render one uncomfortable and do harm.

In hemoptysis of phthisis, digitalin is most valuable when the heart is excited and irregular rather than overly powerful.

The enormous doses of digitalis given by Petrescu for pneumonia are now explained by the weakness of the drug as found in Roumania.

Many practicians believe that digitalis has a specific effect in septic maladies, combating sepsis itself. This has no foundation outside of clinical trials, and not much there.

DIOSCOREIN

Standard granule—gr. 1-6, Gm. .01.

Dioscorein is a concentration from the wild yam, Dioscorea vittata. Its virtues are attributed to a resin, insoluble in water but soluble in alcohol.

King simply says that dioscorea is a specific for bilious colic, giving prompt and permanent relief in the most severe cases. He advised half a pint of the decoction every half-hour, or five drops of specific dioscorea every five minutes. Webster extends its use to every form of colic, to other painful abdominal neuroses, and to all gastrointestinal irritations. If it does not relieve in an hour discontinue the remedy. It allays the pain of biliary calculi when given with gelsemium. It has proved useful in cholera morbus with cramps, neuralgias, nervous irritability with pain or spasms, hiccough, obstinate and painful vomiting, gastralgia, and in a case of asthma (King).

Felter and Lloyd say the action appears to be especially upon enfeebled and irritable mucous membranes, with spasm of their muscular fibers; hence its use in colics, tenesmus of dysentery, spasmodic dysmenorrhea, and gastric spasm with pain and vomiting. It has been advised in indigestion with hepatic derangement, chronic hepatic congestion, chronic gastritis of drunkards, after-pains, etc.

Specific Indications.—Bilious and other colics with spasmodic contractions; yellow skin and conjunctivæ, nausea, colicky abdominal pains, coated tongue, deranged stomach; frequent, small, flatulent stools; colic with tenderness, sharp abdominal pain made worse on motion.

Ellingwood thinks it especially effective in malarial cases, and much more certain in spasm and pain of the bowels, though useful in all spasmodic pains. He advises it in all uterine pains and in ovarian neuralgia.

Shoemaker says dioscorein is expectorant but derives its chief value from its effect on the liver. It is emetic in large doses. It quickly relieves pain and spasm of gallstones if not too large to pass, and is useful to reduce irritation after the passage of the stone.

Hepatic indigestion and its consequences are quickly relieved by dioscorein. Hepatic cirrhosis seems to be delayed by its use, and it increases the analgesic effect of morphine in hepatic carcinoma.

In the treatment of gallstones dioscorein is not a remedy for the intervals but for the paroxysms. In the worst cases the pain is so intense that the most powerful analgesants are requisite, especially glonoin, hyoscyamine and strychnine. But for milder forms, and when the suffering continues after the worst pain is assuaged, dioscorein is a useful resource. From 1-6 to 1-2 grain may be administered, dissolved in an ounce of hot water, every half hour till the patient is easy. While this is not so powerful an

anodyne as others, it is wise to hold these in reserve whenever a mild remedy will accomplish the object.

Dr. J. V. Steele, of Washington, has employed dioscorea in the treatment of gallstone colic, after the worst pain has been subdued by H-M-C. He looks upon tenderness in the region of the gall-bladder as the specific indication for dioscorea, which he administers in full doses until the tenderness disappears.

Dr. M. D. Stine, of South Dakota, advises dioscorein in dysmenorrhea, appendicitis and any painful affection in the abdomen.

The dose of dioscorein in spasmodic and other painful affections is gr. 1-6 to 1-2 every five minutes till relief, best dissolved in a little alcohol or hot water. In chronic maladies give a grain one to four times a day, in granules to secure slow absorption and continuous action.

DUBOISINE SULPHATE

Standard granule—gr. 1-500, Gm. .000125.

While the other alkaloids of this group are derived from solanaceous annuals, this comes from a tree, native to Australia. This alkaloid is also found in minute quantities in belladonna, stramonium and hyoscyamus. Duboisine is isomeric with atropine and hyoscyamine; according to Nothnagel identical with the latter and according to Merck identical with both. Foster says the mydriatic effect is more quickly manifested than that of atropine and does not last as long; that it does not cause delirium like atropine, nor does it disturb the respiration. Cushing thinks the plant and the alkaloid contain at times hyoscine or hyoscyamine.

Duboisine has been recommended in exophthalmic goiter to allay the circulatory disturbance, but it has no control over the course of the malady.

Dr. Cate published an interesting account of its application in a case of Laloneurosis, which will be found in American Alkalometry, Vol. I, page 434.

If there are really differences in these rarer members of the atropine group, they are yet to be demonstrated. According to Merck there are but two alkaloids in this group, atropine and hyoscine, the others being merely mixtures of these two, and modifications that do not materially affect their therapeutic effects. It seems that a fruitful field of experiment awaits the investigator as to the effects of varying proportions of these two alkaloids when administered together.

Heinz says that as a mydriatic and paralyzer of accommodation duboisine acts quickly and more strongly than atropine. The effect subsides more rapidly. In dementia with muscular unrest it seems to act charmingly and induce sleep. He gives up to one milligram internally, or one-third of a milligram hypodermically.

Dr. F. G. De Stone, of California, says: "A young woman, the mother of two children, had suffered from headache almost constantly for three years, having been under some doctor's care all that time. She had been operated upon for laceration of the cervix, but it brought no relief. Every remedy used had failed to help her headache, and she had about decided to stop consulting any more doctors. I decided that there were two things I might do that would do her some good. First, her breath was bad, and I might correct this; second, I felt I might relieve the congestion of her head.

"I gave her the 'clean-up and clean-out' treatment, and ordered a granule of duboisine every ten minutes for six doses and then every hour till the headache had passed. In three days she returned, saying that she thought I could cure her (and that's half the battle). I then examined her carefully, and under the treatment instituted she has not since had another headache, and bids fair to recover perfect health."

Nothnagel gives the dose of duboisine as gr. 1-80 to 1-30, and yet declares it is less than that of atropine. The standard granules of duboisine contain gr. 1-5000, and this may be repeated every ten minutes until the atropine symptoms appear—dryness of the mouth first, then flushed skin, dilated pupils, etc.

In therapeutic applications, effects, toxic and remedial, antidotes, etc., it closely resembles atropine.

ECHINACEA

The best preparation of Echinacea angustifolia as yet available is the concentrated and purified extract.

Tincture of echinacea has been employed as a local application to the glans penis to excite erection.

The reports published on the internal uses of this remedy are sharply divided into two classes—those submitted by men who have applied echinacea in the class of cases for which it is recommended, who are decided and unanimous in their approval of the remedy; and those made by men who have only tested it on animals or human beings in health, or perhaps made a few tentative essays, with unbelief and predetermination to find it worthless. As faith adds

to the effect of any remedy, so its powers may be completely shrouded by unshakable unbelief. Unless the physician is capable of freeing his mind from prejudice and judging dispassionately he should not arrogate to himself the functions of a judge of drug-action.

Lloyd terms echinacea a corrector of depravation of the body fluids. Its extraordinary powers combine those included under the terms antiseptic, antifermentive and antizymotic. It controls the disturbed balance of the fluids resulting in such tissue changes as are presented by boils, carbuncles, abscesses, cellular glandular inflammations; serpent or insect venom, malignant diphtheria, cerebrospinal meningitis, puerperal and other septicemias; "bad blood," asthenia, adynamia, the tendency to malignancy. Septic wounds are treated with this agent. In cerebrospinal meningitis Webster found it best for cases with weak pulse not fast, little fever, cold extremities, headache, peculiar flushing of face down to neck, dizziness and profound prostration. As a stimulant to the capillary circulation he found no equal to echinacea. It endows these vessels with recuperative force. Lloyd doubts the value of this agent in malignant diphtheria, having failed with it. In non-malignant cases it appeared to expedite recovery. It gave him better success in tonsillitis with dirty, ulcerative surfaces. The form of quinsy known in the west as black tongue has responded to echinacea. It aids in the cure of respiratory catarrhs, with offensive ulceration, dark color and debility. It has overcome the fetor of pulmonary gangrene and given early has prevented that catastrophe. Shelley reported a typhoid pneumonia with jet black tongue which improved on echinacea.

Lloyd has used it in fermentative dyspepsia, with bad breath and gastric pain, worse on eating; in duodenal catarrh, intestinal indigestion with pain and debility; ulcerative stomatitis, nursing sore mouth, diarrhea, dysentery, cholera morbus and infantum, typhlitis and perityphlitis; eruptive fevers, especially the catarrhal phases and angina of scarlet fever. It has done best in typhoid and typhomalarial fevers, and in sympathetic fevers from rheumatism or sepsis. King found it fail in every case of ague. Others find it useful in asthenic malaria. It occasionally aids in influenza, and assists convalescence. Puerperal septicemia yields to echinacea but curetting must be done if indicated. The succeeding debility is relieved by echinacea. Hayes commends it in mountain fever.

Echinacea relieves the pain of erysipelas, aiding resolution when the exanthem is extensive, tense and purplish-red; the pain of cancer, especially of the fauces; removing the odor promptly. It

is useful for the cancerous cachexia; for tubercular abscesses, gangrene, empyema with pulmonary gangrene, appendicitis (Farnum); phlegmonous swellings, old sores, erysipelas with sloughing, phagedena, dissecting and surgical wounds, phlegmasia dolens, dermatitis venenata, and to improve the condition of pus cavities.

As a local remedy Lloyd speaks of echinacea for malignant carbuncle, painful mammitis, gonorrhea, syphilis, impotence, purulent salpingitis, offensive leucorrhea, erythematous and erysipelatous vulvitis (Webster), eczema with asthenia and general depravity (physical, we suppose).

Post-scarlatinal dropsy has been reported as cured by echafolta; which is suggested also as preventing hydrophobia. It has been recommended for smallpox, as relieving the symptoms of phthisis, especially the cough of stone-cutters' phthisis; and Lloyd suggests that it may favorably impress the tubercular diathesis.

Specific Indications.—To correct fluid depravation, bad blood, the tendency to sepsis and malignancy, as in gangrene, sloughing and phagedenic ulcerations, carbuncles, boils and various forms of septicemia; for foul discharges with weakness and emaciation; deepened bluish or purplish color of skin or mucosa, with low inflammation; dirty-brownish tongue, jet black tongue, multiple cellular abscesses semiactive with marked asthenia; of especial importance in typhoid, septicemia and other adynamic fevers; for malignant carbuncle, pulmonary gangrene, cerebrospinal meningitis and pyosalpinx; it may be applied locally to annul pain and correct fetor of open cancers.

Ellingwood says that when tincture of echinacea is taken into the mouth it causes tingling, somewhat recalling that of aconite, which remains for half an hour. Swallowed undiluted it causes a sense of constriction and promotes the flow of saliva, followed by diaphoresis and if repeated by diuresis. The functions of all the glands seem to be stimulated. The appetite and digestion improve, the bowels act better, absorption, assimilation and nutrition are enhanced. It encourages secretion and excretion, preventing further autointoxication and correcting what has occurred. It stimulates tissue waste more than any other remedy known. Sallow, pallid and dingy skins become rosy. Anemias improve and gain tone. It is the remedy for blood poisoning. The field covers acute autoinfection, slow progressive blood taint, imperfections of elimination and germic affections. The special indication is the tendency to gangrene and sloughing of soft tissues, throat dark and

full, tongue full with dirty dark brown or black coat, in all cases where there is sepsis or zymosis. As an intestinal antiseptic he places echinacea in the first rank. In typhoid fever treated by it the extreme limit of duration is twenty-one days and some report a week as the limit. In uremic poisoning it will supersede all other single remedies. In cholera infantum it is specially useful when nervous phenomena are present.

Dr. Meyer used echinacea for hemorrhoids, injecting it into the rectum three times a day. He records 613 cases of rattlesnake bite successfully treated by this agent.

Dr. F. M. Friend testifies to the value of echinacea in all cases of sepsis. He employed it in a desperate case of scarlet fever with success.

All accounts agree that there is little if any effect from this drug when given to a person in health. Its effects are only manifested when there is an enemy to encounter. And if it is useless, there are a good many capable observers who have been badly mistaken.

I have applied tincture of echinacea in a series of infected wounds, and all have proved well on the way to recovery next day. It has been claimed that this was really due to the alcohol.

ELATERIN

Standard granule—gr. 1-6, Gm. .01.

This agent is the active principle of the Momordica elaterium, one of the gourd family to which we owe so many valuable medicines. In July the proportion of elaterin is about 0.4 percent, and in August when the plant matures it rises to 0.7 percent. In September it vanishes completely; a circumstance which, as the *Chemist and Druggist* says of a similar variability in hydrastis, does not interest the manufacturers of galenic preparations, but does those who extract alkaloids. Possibly it may interest the physician.

Elaterin is insoluble in water, slightly soluble in ether, readily in boiling alcohol and in alkalies. It requires the presence of bile to develop its activity. It is the type of the drastic hydragog cathartics, acting powerfully on the bowels an hour after it is taken, even more promptly than croton oil.

Besides elaterin, elaterium contains ecbaline, a very acrid and bitter resinoid, profetine, hydroelaterin and elaterid, all ill-known and insufficiently studied. The crude drug causes ulcerations of the hands of those who work with it. Even in moderate doses it causes a condition closely resembling that presented by Asiatic

cholera, with great depression of the forces, and sometimes tetaniform convulsions. When elaterin is given in moderate dose, administered in the usual dosimetric manner—small doses frequently repeated till effect—its action is limited to a more or less prompt and energetic increase of secretion throughout the vast mucous superficies of the gastrointestinal tract. It is strongly hydragog, perhaps cholagog, but does not cause the sharp and painful colics of the crude elaterium. Should slight colic ensue this is readily relieved or prevented by the use of hyoscyamine (Laura).

Elaterin is useful when it is desired to induce a therapeutic intestinal hydrorrhea—in cerebral, bronchopulmonary or hepatic hyperemias, in notable congestions of the portal system, active or passive dropsies, etc. Burggraeve also denied for elaterin the harshness of the crude drug. He advised the former in abnormal dryness of the skin. Laura advised it in the acute hyperemias of infancy, in cerebrospinal meningitis with threatened effusion, and in periencephalitis; also in acute or chronic hydrocephalus. Quette claimed for it a special efficacy in uremia, which Laura confirms.

The medium dose according to Burggraeve is eight granules in one day. For a diuretic action he added digitalin, not more than four granules. Nervous, susceptible persons, liable to colics, should take hyoscyamine with elaterin. When this is to be long continued, as in dropsies, smaller doses are advisable.

Lanphear recommends the pure glucoside to secure very early bowel movement after operation. He gives a milligram every hour till five or six have been taken or copious movements are secured. If emesis results he discontinues elaterin and gives one milligram of eserine hypodermically, every hour, four times. When black vomit begins after operation, this is by far the most effective treatment.

The place of elaterin is in threatened uremia or apoplexy, for the cerebral hyperemia, when it is essential to remove a portion of the toxic material from the blood to prevent convulsions, or to reduce the cerebral vascular tension as rapidly as possible. Here nothing but venesection equals the speedy action of elaterin. These emergencies come to the physician rarely, but when they do come the danger is imminent and haste is imperative. Hence the *vade mecum* case should always contain a vial of elaterin granules, though these need be but few in number.

The standard granules contain gr. 1-6, and of these one should be given every five minutes, or five at once, if possible with an alkali like ammonia to hasten solution and action. Overdoses call for

stimulants and anodynes, hot whisky, hot enemas, camphor and capsicin, with atropine in full doses hypodermically.

EMETINE

Standard granules—gr. 1-67, Gm. .001; gr. 1-6, Gm. .01.

Among the eccentricities encountered by the physician who adheres to the use of ipecacuanha is the uncertain derivation of his supply. Four plants contribute to the ipecac of the market: Cephaelis ipecacuanha, Psychotria S. Ronabea emetica, Richardsonia scabra St. Hilaire, Ionodium ipecacuanha Ventenat. Of these the first three belong to the family of Rubiaceæ, the other to the Violaceæ. The first has about four times the activity of the others.

As early as 1817 Pelletier and Magendie obtained emetine, which they recommended in place of the crude drug, being 100 times as active, and devoid of disagreeable taste and odor. The galenic preparations of ipecacuanha are notoriously unstable and variable in strength, while emetine is stable and uniform, and if the irritant cephaeline is excluded, is far less liable to cause emesis in doses that still fully afford the valuable action on the digestive apparatus to which the principal desirable effect is due.

Emetine does not change when exposed to the air. It is soluble in 1000 parts of cold water, more readily in hot water, and quite easily in alcohol or in ether. It is bitter. It dissolves easily in acids forming acid salts, and is precipitated by vegetable astringents.

The percentage of emetine in the crude drug is so variable that no accurate dosage can be based thereon. Pelletier obtained only 0.78 percent, while Zenoffsky secured 3.8 percent. But Rabuteau declares that the ringed bark contains 16 percent, the striated 9 percent, and the wavy 3 to 4 percent. His method of extraction is as follows: The ipecac is mixed with a little water, potassium or sodium nitrate added, and the emetine precipitates as a nitrate, in a mass; this is washed, dissolved in alcohol, decomposed by milk of lime; the mixture dried in a water bath, powdered and when digested with ether gives up to it all its alkaloid. Evaporating the ether there remains a yellowish substance, which is treated with sulphuric acid. Emetine alone dissolves in the solution, and when dilute ammonia is added the alkaloid is deposited as a white precipitate, which is then washed with cold distilled water. Emetine thus obtained is pure.

Physiologic Action.—Magendie found that half a grain of impure emetine caused vomiting in dogs or cats, often followed by

prolonged sleep. Ten grains caused vomiting in dogs, after which the animals became drowsy; but instead of returning to health as when small doses of emetine were given, the animals died within twenty-four hours. Death was due to a profound inflammation of the lungs and the intestinal mucosa from the cardia to the anus. The same results ensued when emetine was injected into the jugular vein or absorbed from any part of the body.

Two grains of emetine taken fasting by a well man caused prolonged vomiting followed by a pronounced disposition to sleep. One-fourth of a grain sufficed to produce vomiting. Given to a sick man it caused vomiting and stools as with a well man, influencing in a happy manner catarrhal affections, especially when chronic. Huesemann found that emetine produced a cathartic effect not obtainable from ipecac, in which the crude vegetable matters hinder this action.

Applied to the skin in ointment emetine causes after some time a sense of burning, forms pustules with a red areola, and induces continual anorexia. If its local application is continued long enough it causes ulceration of the skin to which it is applied. Introduced in the eye it causes inflammation of the conjunctiva and cornea; in the nose incessant sneezing; in the air passages cough, swelling of the mucosa and respiratory troubles (Buchheim). A concentrated alcoholic solution left in contact with the tongue produces a sense of warmth quite different from that caused by aconitine or by veratrine. Injected under the skin it causes local inflammation which renders this mode of administration unavailable. If thus used it occasions vomiting as when given by the stomach.

Emetine is eliminated by the gastric mucosa and by the kidneys (Dragendorff). The local action on the gastric ends of the pneumogastric causes a secondary excitation of the vomitive center, for Pecholier and d'Ornellas found that the emetic action was suppressed by section of the vagus.

The nausea is more decided when the drug is introduced through the stomach.

A very light dose—gr. 1-134 to 1-67—by the mouth, causes a slight sense of warmth in the stomach, like that following a small dose of arsenic. A larger dose repeated, gr. 1-30 to 1-12, causes yawning nausea, free salivation and sometimes vomiting. Meanwhile the bronchial and intestinal mucous secretions are increased. Still larger doses cause prompt vomiting, followed, as are moderate doses if repeated, by liquid stools. Collapse and death may result if the doses are large enough. Rutherford introduced ipecac

directly into the duodenum of dogs and observed an increase in the secretion of bile and of the intestinal mucus. The pulse is accelerated by an emetic dose up to the occurrence of vomiting; it then falls even below normal. If vomiting does not occur the heart action is retarded. Toxic doses can cause death by cardiac paralysis. The effect on the respiration is quite similar.

Emetine has no direct influence on the central nervous system. It causes muscular depression. During the nausea the cutaneous glands are active. Therapeutic doses have no appreciable effect on the urinary secretion but toxic doses may cause albuminuria.

Emetine is said to occasionally cause hyperemia or œdema of the lungs; to dissolve the red cells when injected intravenously; and sometimes to cause urticaria when taken by the mouth. Shoemaker is quite positive as to its cholagog action. At any rate, when given in a single full dose at bedtime and retained, the evacuations next morning are those usually denominated bilious, and the effects are such as are attributed to clearing out of this organ. In fact, it has seemed to the writer that not even calomel so completely unloads the liver.

Van Renterghem says that except violine emetine has no *synergist.* All emetics are auxiliaries. Pilocarpine sometimes causes vomiting, but it is ranked with emetine rather for its action in increasing the secretion of the bronchial mucosa.

The narcotics retard the nauseant action, as well as the purgative; while the aromatics and stimulants do this and also combat the general depression and tendency to collapse. Cocaine as a local anesthetic, and the strychnine group as incitants of the nervous system, prevent or retard the nauseant effects of emetine, but act as auxiliaries when one desires the other effects without the nausea.

The only *antidote* is tannic acid, which precipitates emetine as an insoluble tannate. Gallic acid and all the vegetable astringents, iodine, iron and lead, are chemically incompatible with emetine.

Sollmann says that cephaeline is by far more emetic than emetine, less nauseant and less depressing to the heart, more irritant to the kidneys, and somewhat hemolytic.

Therapeutics.—Emetine fills the multifarious role of an emetic, expectorant, digestive, antispasmodic, hemostatic, diaphoretic and defervescent.

As an emetic it is mild in action and the nausea does not long remain after emesis. It is specially valuable when the indication is to relieve the stomach of undigested food. For children emetine is useful as it depresses less than most other emetics.

The nurse should be warned that sometimes the vomiting does not occur, and that the remedy should be suspended when the bowels act or symptoms of depression occur.

As an expectorant emetine is indicated when there is a deficiency in the bronchial secretion, or when the latter is tough and adherent. Dry cough calls for emetine. This is the case in the early stages of acute bronchitis and laryngitis; and in chronic cases with scanty secretion. When the same condition is present in early phthisis emetine may be given. In spasmodic asthma emetine must be pushed to nausea for benefit to accrue. In whooping-cough it is usually given in the catarrhal stage, with little if any benefit. In fact, the failure of such remedies usually first arouses the suspicion that we have to deal with this malady.

As a digestive emetine is useful in all cases where the digestive fluids are deficient. In very small doses, well within the nauseating limit, it is well suited to gastric and duodenal catarrhs, and to the dry forms of ileocolitis. In most forms of acute intestinal irritations, simple diarrheas, cholera infantum, cholera morbus, whenever the intestinal secretions are vitiated and unhealthy, the stools unduly fetid, emetine promotes the secretion of healthier products. In dysenteries of the graver types, tropical, foudroyant, it is a specific. Given in doses of one-tenth grain of the chemically pure alkaloid, or one grain of the brown amorphous emetin, with every precaution to prevent vomiting emetine exerts a degree of control over this malady not approached by any other remedy. The patient should be prepared for the night, be put to bed, and then take the dose in tablets or capsules, which must be swallowed whole and dry, with no fluid; he then must lie perfectly quiet for half an hour, and before the expiration of this time he will usually be asleep.

When he awakes in four to eight hours he will be markedly improved. If the dose is vomited it should be at once repeated. Sometimes it will be necessary to first administer a small hypodermic of morphine to insure the retention of the emetine.

Emetine in similar doses administered in the same manner constitutes one of the most effective remedies for delirium tremens. Many times I have given a grain of brown amorphous emetin at bedtime to a patient in the beginning of such an attack, and wild with the incessant craving for whisky; within thirty minutes he would be asleep, and after eight hours' rest, awake free from the craving, and ready for his food. This dose produces one or two spinach-colored stools, and if it does not act on the liver there is at least every appearance of such action.

To obtain antispasmodic effects from emetine it is necessary to administer it in nauseant doses, sufficient to produce muscular relaxation. Given thus it has proved of use in uterine spasm, etc. But the most important application in this group is to the spasms of childhood, usually dependent on unwholesome food and relieved by emesis. Repeated spasms with muscular relaxation form the picture of a case suitable for emetine.

The hemostatic effect is due to the relaxation of arterial tension, and also requires nauseant or emetic doses. But as vomiting itself may favor the hemorrhage the object is to secure relaxation without pushing to the emetic dose. This can easily be accomplished by the intensive method of rapidly-repeated minute doses, stopping the moment nausea is felt.

As a diaphoretic emetine is not of much importance, pilocarpine being immeasurably more powerful. There are few conditions in which Dover's powder is not advantageously replaced by the latter.

The antipyretic influence of emetine does not depend on a direct action upon the pulse rate or the temperature, unless it is given in toxic doses. The effect is rather to be attributed to the opening of the excretory channels, allowing the materies morbi to pass out of the body. This is best shown in pulmonary inflammations, when emetine is given in doses sufficient to promote secretion and relax tension. Emetine goes very well with the defervescent alkaloids, veratrine and aconitine, but antagonizes digitalin to some extent. As a diaphoretic ipecac has always been administered with opium, as in Dover's powder. The writer has modified this old favorite in accordance with modern therapeutics, by using emetine and codeine, with camphor monobromide. This forms an excellent combination for a diaphoretic, sedative, hypnotic and soothing remedy for dry irritative coughs. It has less tendency to nauseate and constipate than the old Dover's powder, and is more speedily effective and manageable.

For use in chronic constipation and other chronic affections of the alimentary canal emetine is administered with aloin, atropine, strychnine and capsicum, sometimes adding physostigmine for flatulence, or podophyllin to affect the liver more decidedly. For gastric affections, especially of infants, an excellent combination consists of emetine, rhein or juglandin, and sodium carbonate and sulphocarbolate, with aromatics. Innumerable combinations are made of emetine with other remedies; in fact, it is far more frequently thus used than alone.

In India the treatment of the severe dysenteries common there by ipecacuanha has become an established method. Many experiments have been made with ipecac deprived of its emetine, since it is recognized that the best results are not secured if vomiting follows. On the whole the evidence is not conclusive as to the superiority of the deemetized drug. Clinical trials by the writer show a great advantage in the use of amorphous emetin, which has been freed from cephaeline, the acrid emetic principle of ipecac root. I have taken a grain of this in whole tablets with no nausea whatever, though one-twelfth of a grain in warm solution will nauseate me promptly. Chemically pure emetine will nauseate in doses exceeding gr. 1-11.

As an adjuvant Laura finds it useful in gastric and duodenal disorders, or even in those of the small intestine, with alternating constipation and diarrhea, such as frequently occur during the progress of febrile maladies, especially in infancy. In mild hepatic engorgements with defective secretion of bile, emetine may usefully be given with quassin and caffeine. It is useful in chronic diarrheas, and in those of infants that recur on slight provocation. In bronchorrheas it may be associated with calcium sulphide, tannic acid and cubebin (Laura).

Burggraeve gave as a contrastimulant one or two granules, each gr. 1-67; as an expectorant six to eight granules a day. Three to ten of the French granules suffice as an emetic dose for adults. To incite mucous secretion give one granule every one or two hours. This dose suffices in dry catarrhs.

Emetine is especially useful as a cholagog that does not purge. It may be so given as to restore the biliary secretion without any catharsis whatever, and the secretions it incites are normal in character. It is therefore an incitor rather than an excitor. In alcoholic subjects emetine is probably the most valuable drug at our command, subduing restlessness, eliminating toxins, inciting healthy digestive secretions, inducing normal sleep, and quelling the fierce craving for liquor.

The employment of the active principle, emetine, is destined to be largely increased, as the substitution of Carthagena ipecac renders the official preparations of that root more irritant than those derived from the Brazilian plant.

Shoemaker enumerates the following uses for ipecac: Locally, as a remedy for insect bites, 2 parts to 15 each of alcohol and ether; also in watery solution for rhus poisoning; and the wine of ipecac sprayed into the air passages for emphysema, fibroid phthisis,

winter cough and chronic bronchitis (Murrell); internally very small doses for nausea and vomiting, of pregnancy or of alcoholism; full doses for hemoptysis, epistaxis and metrorrhagia; to overcome uterine inertia in the first stages of labor; to free the bronchi of secretion in whooping-cough or in capillary bronchitis; pushed to full tolerance in epilepsy (Bond); dram doses of the powder for cholera morbus and Asiatica; tuberculous diarrhea and night-sweats; torpor of the liver; flatulent dyspepsia; to stimulate the liver in malarial poisoning; catarrhal jaundice; laryngismus stridulus; puerperal hemorrhages and dysenteries (Trousseau); hematemesis (Burland).

King says the specific indication for ipecac is the presence of irritation, even enumerating mental and nervous irritation in his list. His chief indications are: Elongated and pointed tongue, red tip and edges, large or effaced papillæ; tenderness on pressure; contraction of tissues; pinched countenance, white line around mouth, tendency to nausea and vomiting, with or without eructations, and marked hyperesthesia. Hyposecretion, capillary engorgement, cases acute. These indications presenting in gastric, enteric or pulmonary maladies call for ipecac, or better for emetine. Hemorrhagic cases calling for ipecac are nervous individuals with marked irritability and vascular excitation. Bleeding hemorrhoids are sometimes benefited by this remedy.

A. L. Blesh has sometimes succeeded in having the grain dose of brown amorphous emetin retained in cases of dysentery by first partially anesthetizing the stomach with a single large dose of cocaine. At other times a large precedent dose of carbolic acid has accomplished this object.

G. M. Jameson of Buda, Texas, praises emetine for the dry cough of severe forms of measles. He gives gr. 1-32 to 1-16 every half-hour to one hour.

Blake (*Merck's Archives*) claims that ipecac in full doses energizes the circulation, accelerating the blood-current but lessening its volume, the vasomotor spasm in the skin accumulating the blood centrally, causing congestion and albuminuria. The skin cools and the heat rises internally. In bad hygienic conditions with weak digestion and faulty elimination small doses of ipecac are curative by stimulating ganglionic energy, hastening circulation and promoting the nutritive processes, also by stimulating elimination. In croup it loosens the membrane by the thin mucous secretion exuding under it. In spinal exhaustion, from over-exertion, heat or teething, the blood is centralized, the solar plexus irritated, and vomiting and

purging result. Very small doses of ipecac frequently repeated, direct the blood to the surface and relieve alimentary congestion. By increasing capillary innervation it checks choleraic discharges, menorrhages, syncope, and diseases of old age, and causes uterine contractions.

Dosage.—If nausea or emesis is desired emetine should be administered in warm water; but if the effect on the liver or the hypnotic action is indicated, or if for any reason it is best that the remedy should not be vomited, the granules or tablets should be swallowed whole and dry, that absorption may be slow. As a diaphoretic and for most uses the dose is gr. 1-67 of amorphous or gr. 1-250 of pure emetine repeated every five to sixty minutes, or less frequently. In dysentery and delirium tremens from gr. 1-6 to gr. j of the brown, one-tenth these doses of the pure, is the dose, and this may be repeated every eight to twenty-four hours.

When emetine is administered hypodermically it excites vomiting but not so promptly as when taken into the stomach. Laura advises emetine in diarrheas becoming chronic and habitual, and in infants when diarrhea occurs on slight provocation. Magendie used it in such cases. Laura advocates it in chronic bronchitis, with calcium sulphide, tannic acid and cubebin when indicated.

R. A. Black reports the successful use of emetine in very small doses, for constipation in infants.

ERGOTIN

Standard granule—gr. 1-6, Gm. .01, and tablets gr. 2, Gm. .13.

Ergot, ergot of rye, Secale cornutum, is the sclerotium of a parasitic fungus, Claviceps purpurea, which replaces the normal grain of rye, Secale cereale. The market supply is derived chiefly from Russia, Germany and Spain. Some attempt has been made to replace the standard article with corn ergot but the latter has not proven satisfactory. Ergot in its natural condition is horn-shaped, about an inch in length, externally of a purplish black and upon fracture white with a pinkish streak. The odor is disagreeable and peculiar and the taste oily and nauseous.

This body has different active principles and its chemistry has even at this late day yet to be fully settled. Ergotinic acid, cornutine and sphacelinic acid are three impure bodies which have been separated but none of these represents properly the activity of the entire drug. Ergotinic acid is toxic and if injected intravenously causes ecchymoses and wide-spread inflammation; cornutine often

causes convulsions and sphacelinic acid causes gangrene. Quite recently Jacobi has isolated sphacelotoxin which he claims represents the active principle of sphacelinic acid. The preparations of the drug are many. The fluids are variable in potency; some are inert and the best are often unfit to be injected subcutaneously. The fluid and solid extracts are largely used and the varying reports as to the efficiency or uselessness of the drug are due to the different preparations used.

Ergotin, which alone is used alkaloidally, is a purified hydro-alcoholic extract of ergot and gives in practice the most even and certain results. This preparation is not affected to any marked extent by age or exposure as is every other form of ergot. It may be given internally or hypodermically with equally good effect and abscesses do not follow its exhibition in the latter manner.

In 1884 Kobert discovered cornutine in ergot. It is an alkaloid, amorphous, little soluble in water, but the salts are easily soluble. Kobert and Lewitzky attribute to cornutine the specific action of ergot on the uterus. By irritating the uterine center in the lumbar cord it evokes arrhythmic contractions of that organ. In non-pregnant animals these contractions only occur in late stages of poisoning by cornutine, but in pregnant animals the uterus is first affected. The pains are more violent the nearer the animal is to full term. Tetanoid contraction of the uterus was not observed, even after large doses.

Toxic doses cause convulsions, by centric irritation. Small doses increase the reflex excitability of the cord, while large doses paralyze it. Very small doses slow the pulse by irritating the pneumogastric, and very large doses paralyze it. The blood-pressure is vastly increased. This is followed after large doses by paralysis of the vasomotor center and a corresponding fall of the pressure. The striated muscles are also affected causing stiffness similar to that caused by veratrine. Lethal doses cause death by paralyzing the respiratory center. Both stomach and bowel contract powerfully under cornutine.

Another body was discovered by Kobert in ergot, to which he gave the name of sphacelinic acid. This produces gangrene; and one of the advantages of employing cornutine is that this acid is thereby left out.

Lewitzky says cornutine is the surest means of exciting uterine contractions, whether the organ is pregnant, or enlarged from chronic metritis, or after abortion. The indications are therefore the same as for ergot.

Meisels used cornutine successfully for urethral and vesical hemorrhage in paretic spermatorrhea. The citrate is preferred. Dose, gr. 1-33 to 1-6. It is not well suited for hypodermic administration. Cornutine keeps better than other ergot derivatives, especially when kept dry. The price is as yet too high for extensive use.

Sollmann says that cornutine seems to act purely on the medulla, its effects resembling those of picrotoxin. It raises vascular pressure, by a central action, without the preliminary fall of ergot. It does not act directly on the heart, but on skeletal muscle like veratrine. Santesson denies that the ergot alkaloids are concerned in the action on the uterus or in inducing gangrene, which he attributes to the resins.

Until the cost is within reason the best preparation of ergot accessible is Bonjean's ergotin, a watery extract. When prepared by the best makers this is fairly uniform and active. It has the very great advantage of being readily used hypodermically.

Acute poisoning by ergot has been noted after attempts to secure abortion. The symptoms are collapse, weak, rapid pulse, tingling, itching and coldness of the skin, unquenchable thirst, vomiting and diarrhea, confusion or unconsciousness, uterine hemorrhages, abortion and jaundice. Subcutaneous and internal ecchymoses were found (Cushny).

Chronic poisoning from the use of ergotic rye is still seen in Russia. The symptoms fall into two groups, the gangrenous and the nervous.

The gangrene occurs in the fingers and toes, extending along the entire limb, which is cold, anesthetic, dusky, then dry, hard and shrunken, falling off with slight pain and no hemorrhage. In mild cases only the skin is affected. Internal necrosis may occur, causing cataract, or ulcers of the bowel, stomach, lung or uterus. Abortion is uncommon.

In the neurotic form there are depression, weakness, drowsiness, headache, giddiness and paresthesiæ. Paroxysmal convulsions occur, clonic, epileptiform, followed by contractures of the limbs, sometimes of the trunk. Mental debility even extending to dementia may ensue.

Vahlen in 1904 isolated a principle designated as clavin, to which he attributes the power of inducing uterine contractions but not convulsions or gangrene. It is soluble in water. Should this be produced commercially it may replace ergotin with advantage. Sollmann says that the active principles in the crude drug decom-

pose very rapidly, and it must be renewed annually. The extracts seem to keep better. The action he attributes to sphacelotoxin, whose effects he summarizes: Stimulation of unstriped muscle, contractions of the uterus, vasoconstriction, gangrene after large doses, cardiac depression followed by stimulation if rapidly injected, vomiting and increased peristalsis, circulatory changes in the central nervous system, and paralysis of the vasoconstrictor ends by large doses. When given to the rooster the effects on the comb are evident in about an hour. Experimentally it has been found that the pulmonary vascular pressure is raised by ergot, and Sollmann apparently contradicts himself by attributing the benefits from it in asthma to its obviating a pulmonary vasodilatation.

Physiologic Action.—There exists a wide difference of opinion as to the physiological action of ergot. We know, however, that it increases parturient action; that in moderate doses it constricts the arterioles in various portions of the body, and as a result arterial pressure is somewhat raised. The drug has a stimulant effect upon the vasomotor center and probably also a direct effect upon the muscular coats of the blood-vessels. It is not always suitable for prolonged administration as it has a tendency to produce gangrene.

Given hypodermically or intravenously in medicinal doses, the blood pressure is first lowered and then raised, the preliminary fall being supposedly due to temporary depression of the heart muscle from direct contact with the drug. Given by the mouth its action is rapid; within thirty minutes, often, its effect is apparent and the impression lasts fully an hour. In emergencies (postpartum hemorrhages) from 2 to 5 grains may be given, preferably hypodermically. A fresh solution should be made at the bedside and the solution may be filtered through sterile gauze if time allows. In severe floodings the dose may be repeated in half an hour and as ergot is really as far as obstetric indications are concerned an emergency remedy, the accoucheur should provide himself with a supply of a reliable preparation. Many of those upon the market are absolutely inert.

The accounts given of the action of ergot, therapeutic and toxic, are so contradictory that little value is to be attributed to them. It is evident that the various preparations of this drug vary greatly as to the nature and proportions of their active constituents. No definite effect is to be expected from such uncertain agents. For instance, many observers credit ergot with the power of causing uterine contractions and an equal number deny that it can initiate

these movements. Most physicians believe that it causes tetanic contractions of the uterus after parturition has commenced, but others deny this. It would seem that an agent so uncertain had better be left out of practice; but if the desired effect can surely be obtained from ergotin, there is no reason we should deprive ourselves of its great benefits.

Ergot has been applied locally for gonorrhea, acne, rosacea, conjunctivitis, endocervicitis, and incipient boils (Shoemaker); also for hemorrhoids, prolapsed rectum, relaxed sphincter ani or vesicæ; but there seems much doubt as to whether an agent acting upon the centers as ergot does, can exert any local action beyond suggestion. T. Clemens gave ergotin by the stomach and injected it into the bladder (4 grains to the ounce) for ammoniacal cystitis of paraplegics, with advantage.

Every variety of hemorrhage has been stopped by ergot in sufficient doses, though Binz denies its efficacy except in uterine hemorrhages. In these it has been the writer's experience to find the bleeding reduced by ergot to a mere dribble, but this refused to stop even when the drug was given till the legs grew cold and the pulses at the ankle were imperceptible. But when digitalin was then given the remaining hemorrhage ceased. This was in post-partum bleeding. When the hemorrhage is from uterine tumors, polypi or fibromyomas, there is evidence that ergotin checks the bleeding and reduces the growth by cutting off its blood supply and constringing the uterus. Mechanical means may be employed to facilitate the separation and extrusion of the tumors.

In labor when there is a history of previous floodings, it is customary to give a full dose of ergot just as the child's head is ready to be born—presses upon the perineum, the latter dilated properly.

In uterine subinvolution Hirst recommends ergot with strychnine and quinine.

Night sweats, hyperidrosis, and galactorrhea, have been treated by ergot. In purpura it is usually given, but the writer has never witnessed any good effect from it. In relaxed states, as in diarrheas, dysenteries, passive pulmonary congestions, etc., ergot may be of value, but strychnine fills this indication so well that nothing else is needed.

In diabetes insipidus the outflow of urine is controlled to some extent by full doses of ergotin, and it has been used in glycosuria also. The powerful vasoconstrictor effect of ergotin has been utilized in treating congestive dysmenorrhea and migraine, spinal hyperemia, vesical paralysis, whooping-cough, etc. It has been in-

jected hypodermically for varicose veins, varicocele, enlarged spleen, and hemorrhoids. In acne when enough ergotin is given, the malady completely disappears, but returns when the ergot effect passes off.

Ergot in full doses has been advised in many affections of the nervous centers, brain and cord, such as spinal hyperemias, paraplegia, chronic mania with hyperemia, in fact in any hyperemic malady of these tissues.

Paretic spermatorrhea is said to have been benefited by this drug.

Gossypin, hydrastine, physostigmine and pilocarpine cause uterine contractions and are synergists of ergotin in that respect.

Digitalin, hydrastine, atropine and hydrastinine, are synergistic as hemostatics.

Ergotin has been given to restrain too free mucous discharges, leucorrhea, etc. It has been injected hypodermically over aneurisms with benefit. In a case of pulsation of the abdominal aorta where ergotin was employed by the writer under the mistaken diagnosis of aneurism, recovery ensued.

The dose of ergotin by the mouth is gr. 1-6 to j, repeated every hour, more or less, as needed. In acute hemorrhages or to stimulate the uterus it may be given hypodermically in single doses of three grains every four to eight hours. In nervous maladies Wood gave fluid extract of ergot in doses of a dram to an ounce; but this preparation is so uncertain that little definite information as to dosage is to be derived from it.

The effects of ergot are not manifest for some hours after administration.

Dr. Alfred P. Livingston has for years made a special study of ergot; hence his conclusions are of exceeding value. His observations relating to ergot are derived from its obstetric uses. The general deductions which he thinks warranted from his personal experiences are:

1. Its direct and specific effect is the contraction of unstriated muscular fiber or other involuntary contractile tissue. Here he comes into direct opposition with those who have recently stated that ergot is not useful but harmful in cerebral hemorrhages, because it cannot act on the muscular fibers of the cerebral arteries, since they have no muscular fibers. Dr. Livingston says that no other effect of ergot has more positively been demonstrated than the relief of congested states in the brain. It must therefore act upon some other contractile tissue besides the unstriated muscular fiber.

2. It does not markedly contract that which is normal in tone.

3. It is emphatic in its contraction of that which is lacking in tone.

4. It is striking in such effect in proportion to the recency of occurrence of the atonic state in such fiber.

5. Its widest field of usefulness is its application to the muscular coats or other contractile tissue of weak and relaxed blood-vessels.

6. It there tends to equalize vascular tension, etc., to distribute the blood equally throughout the body, to restore or promote functional activity of glands and organs generally and vasomotor centers particularly, to promote sleep, to relieve pain, nervousness and spasm, to prevent or modify the effects of autotoxins and bacteria, to promote assimilation, absorption of exudates and elimination of waste, to relieve nausea, to prevent the ill and dangerous effects of anesthesia, to promote the healing of wounds, to prevent or modify inflammation, to arrest capillary hemorrhage, to relieve narcotic poisoning, and to make the work of the heart more easy and so to prevent its exhaustion or paralysis.

7. It is useful to restore tone in the unstriped fiber of the walls of the hollow viscera, stomach, bowels, bladder, uterus, etc.

8. The prevalent popular notion existing in the medical profession that it is a dangerous drug and likely to produce ergotism, is unfounded as regards the modern pharmacopeial preparations, at least as regards such as he has used during the past thirty-four years.

9. Its local action upon the stomach is often offensive, especially if full doses are given; its absorption from the stomach is uncertain, both as to promptness and degree, and therefore,

10. Its administration should be limited as much as possible to hypodermic injection, which assures immediate effect, admits of exact regulation of dose, and avoids nausea and other ill effects of its administration per os.

These deductions, Dr. Livingston tells us, are wholly founded upon his clinical experience. This he considers the only reliable guide as to the applicability of any therapy to disease. The indications for the application of ergot, therefore, he considers to be the recognition of lack of tone in unstriped muscular fiber or other involuntary contractile tissue; and on that single thread he hangs all the manifold indications for ergot, and its myriad utilities in therapeutics.

From this Dr. Livingston goes on to produce a remarkable array of indications for the administration of ergot. Practically, his indication is loss of balance of circulation, for if spasm of the blood-vessels exists in any one part, with local anemia resulting, he looks upon this as evidence of weakness of the contractile coats of some blood-vessels, and so gives ergot. If the walls of the blood-vessels are unusually weak or greatly strained he gives ergot. Inflammation of limited areas he treats with ergot. Atony of the hollow viscera, disorders of assimilation and elimination associated with the minuter circulation, impaired functional activity, he looks on as an indication for ergot. In fact, if there is too much blood or too little in any one part, ergot is given.

He thus gives a tremendous range to his favored remedy. In truth, it seems difficult to exclude anything if we allow the correctness of such premises. Dr. Livingston apparently gives to ergot the place which strychnine holds with a large number of the medical profession. Strychnine energizing every function and every tissue in the body, should necessarily be indicated whenever there is detected a lapse of functional activity in any part. But, then, do we not take the broad ground that illness of any description is indicative of a lapse in functional activity of one or other part of the body?

We cannot believe with Dr. Livingston in his universal application of ergot, nevertheless there is a great deal to be learned from the observations made by this excellent clinician, who has studied this drug for a life-time in the field of clinical therapeutics.

As symptoms of chronic ergotism one writer mentions itching feet, backache, muscle cramps, vertigo, intense cold and aching in limbs, apathy, abortion, loss of sensation and dry gangrene; or, vomiting, diarrhea, itching, anesthesia, ravenous hunger, tetanic spasms of flexors, tremors, vision disturbed, convulsions, delirium.

Therapeutics.—In all bleedings from the uterus, whether due to fibroids, cancer or parturient accidents, ergotin is our most useful remedy when pure. In fibroids the drug should be given in smaller doses, either by the mouth or by hypodermic injection. The treatment should be continued for weeks. There is a marked reduction in the size of the tumor and often it seems to become absorbed. In the worst cases it ceases to increase in size.

In the parturient woman small doses induce uterine contractions closely resembling the normal. If full doses are given, however, these become powerful and tetanic. As there is a vast difference in patients' tolerance of this drug, it is difficult to estimate what will be a safe dose. It has therefore become a rule never to

administer ergot until delivery has been accomplished. A full dose will then often expel the placenta and cause firm contraction of the uterus. When after the third stage the uterus remains flaccid and "boggy" two or three moderate doses of ergotin (gr. 1 to 2) will cause a marked change for the better. It is a mistake, however, to give ergot as a routine measure as so many practicians are in the habit of doing. In cases known to be post-partum "bleeders" a full dose may be given after the head is born. In subinvolution it is a useful remedy but the possibility of affecting the nursing child should be borne in mind.

Ergotin has proven of undoubted service in metrorrhagia, gr. 1-6 to 1-2 being given every two hours till effects are produced. In hematemesis, hemoptysis and hematuria its use is questionable; in hemoptysis especially it would seem to do more harm than good.

Ergotin causes contraction of the sphincter vesicæ and this often produces annoying symptoms; it is evident that it should be a reliable remedy in incontinence. It may be combined with strychnine with advantage. Wherever it is desirable to contract involuntary muscular fiber, there ergotin is indicated; and as the smaller blood-vessels are largely formed of involuntary muscle fibers it may be given to lessen capillary blood supply. It would be indicated in congestive headaches—especially in those of a full habit—but as it acts most powerfully on the splanchnic vessels the effect of full doses may really be to increase cerebral congestion.

Ergotin has also been used with success in diabetes insipidus and colliquative sweats. Various writers have also recommended it as a useful remedy in diabetes mellitus, meningitis, myelitis, splenic enlargements, acute dysentery and skin diseases. In all of these, however, with the possible exception of splenic enlargement, it has proved unsatisfactory.

Ergot remains what it has always been, the obstetrician's best friend. Its action upon the uterus is prompt and powerful and, if a reliable preparation is used in sufficient quantity, the desired effect can always be obtained. Given internally ergotin may produce nausea but this form of the drug is less objectionable in this respect than the fluid extracts.

In giving ergotin hypodermically the solution should not be thrown under the skin but deep into muscular tissue. In this manner the formation of abscesses is almost positively avoided. Quinine, hydrastin, gossypin, can in certain instances take the place of ergotin to some extent. Some practicians are in the habit of administering a full dose of quinine as soon as labor sets fairly in

and giving a dose of ergotin as soon as or immediately after the head is born.

Ergotin has been recently recommended as an efficient remedy in puerperal fever. It has been used not only as a specific but as a prophylactic. In a series of thirty cases Solt used ergotin throughout the sickness and says every case recovered with a rapidity never before witnessed. Other observers support this claim.

The benefit is due to the action of ergot in forcing the decomposing infected debris out of the uterus, and closing its vessels against further absorption.

Moderate doses for a prolonged period have been suggested in multiple sclerosis.

In all cases of disordered circulation ergotin, it is suggested, should be given hypodermically. It is capable of restoring tone and equilibrium to the circulation; many writers have recently asserted that it is more valuable than most of the accepted heart tonics. Its administration by the mouth is condemned. Large doses given hypodermically have been warmly recommended in all acute inflammatory infections. Meningitis, pneumonia, pericarditis and erysipelas are among the diseases enumerated as being successfully treated with ergotin. It has also been found to relieve the serous apoplexy of alcoholics and is useful in pulmonary edema. In conjunction with strychnine, ergotin is recommended in chorea. The convulsive condition is ameliorated and the general tone of the patient improved.

Nagel says that ergot begins to act within fifteen minutes, attains its maximum in thirty minutes and the effect lasts one hour.

Laura gives ergotin with cicutine for the pains of cancer, and applies it topically to arrest capillary hemorrhages and favor healing of unhealthy wounds. He considers it a dangerous remedy in abortion when the fetus is dead and the placenta detached, whilst if given after the uterus is empty it favors involution. As a hemostatic in uterine cancer it is of only temporary benefit. Langenbeck, Albanesi and others used it with success for aneurisms, and Ciattaglia injected it into varicoceles. Laura suggests its employment in inflammations with acute cardiovascular excitation, functional cardiac hyperexcitation, whooping-cough, pulmonary tuberculosis, mild bronchites, bronchiectases and mild pneumonias, atonic dilatations of hollow viscera, with or alternant with brucine or strychnine, and in the latter combination in lead palsies. Hertmann applied it locally for urticaria and pruritus. Yeats succeeded with this remedy in mania and in epilepsy; others in hemicrania and

prosopalgia. Dujardin-Beaumetz said that when ergotinine was injected hypodermically in doses of more than gr. 1-12 it always induced colics and vomiting; while the hemostatic action only developed in twelve to twenty-four hours. It is slower than atropine, not so slow as digitoxin.

Houdé advises ergotin in a long list of ailments. Its vasoconstrictive action may be utilized in a number of hemorrhages; in active and passive congestion of the uterus, chronic engorgements, cerebral hyperemia, paralysis, mental diseases, apoplectic coma, and myelitis; it will calm the sufferings of a tubercular meningitis; the action of ergotin on muscular fiber is available in visceral atony, of the bladder, of the rectum with prolapsus, retention or incontinence of urine, uterine fibroma, atony and dilatation of the stomach; its moderating action on the secretions makes it useful in polyuria, diarrhea, dysentery, and night sweats; it has also been proposed in aneurism, dyspepsia, goiter, hemorrhoids, congestive neuralgias, true diabetes, and blennorrheas. It manifests its good qualities in mental ailments, such as melancholy, hypochondria, dementia, also in late paralyses, and in paralysis of the bladder and rectum. It has sometimes succeeded when electricity and strychnine failed. With some uterine tumors it seems to act not only by stopping bloody discharges but arresting the development of the neoplasm by cutting off its blood-supply. Retrogression occurs occasionally.

Dr. J. Darwin Nagel says: "Ergot until recently has been little used in general therapeutics. With the exception of obstetrical conditions, demanding the employment of a quick hemostatic, it is only of late that physicians have essayed the use of ergot in various conditions of impeded blood circulation, and the consensus of opinion of all those who have tried the drug in its pure state by the hypodermic method, seems to be, that in ergot we have a drug of the highest potency and perhaps of more varied usefulness than opium itself.

"Up to within a few years, the successful use of ergot has been greatly limited by our inability to obtain a preparation that gave uniform results, but since the introduction of ergotin and its hypodermic use, we have been enabled to get exact results and thus regulate the dosage of this all-powerful drug to suit our purposes. Ergotin is the most satisfactory of all ergot preparations. It is prepared by dissolving five parts in seven each of glycerin and water and it is then filtered. The ordinary dose is from three to twelve minims (representing 120 grains of crude ergot) but I have often given as high as 45 or 50 minims at one injection.

"In using ergotin, we should always remember the following rules:

"1. The solution should be fresh, as ergotin never irritates the tissues unless it has begun to decompose.

"2. The injection should be given in the back or the hips.

"3. In dissolving the ergotin, use distilled water only.

"Ergotin is a powerful stimulant of the vasomotor centers, causing a tonic spasm of the muscular walls of the blood-vessels, accompanied by a rise of arterial pressure and a slowing of the heart beat. Toxic action is rare in human beings. In some instances, where too much ergot has been used for a protracted length of time, we observe a depression of the heart action which in some cases produces paralysis of the vasomotor apparatus, ending either in convulsions or in gangrene; but a fatal outcome from the use of ergot has been so rare that it can be left entirely out of our consideration.

"Until recently, ergot has been used mainly in labor. It has little action on the normal uterus, and should be used in labor only after expulsion of the placenta. It has also been used in inertia following abortions; in hemorrhages from neoplasms, but not in hemorrhages of cerebral origin. It is also used in alcoholism and in hemorrhages from typhoid fever; in spermaturia, diabetes and enlargement of the prostate. But my article today does not concern itself with the general uses of ergot, but with its wonderful effects in septic conditions, particularly so of the peritoneum.

"In looking over the literature on the use of ergot I find very little mention made of the value of ergot in septic conditions of the system, but the universal success which I have obtained in conditions where surgical interference is inadvisable, inappropriate or dangerous, has been such that during the last two years I have become the most enthusiastic advocate of the use of ergot in all conditions where sepsis prevails, whether the knife has previously been used or not. Its action in such cases seems to be prompt, rapid and exact, and in some instances the results are really marvellous. It evidently produces its effect by the powerful contraction of the muscular coats of the congested and dilated blood-vessels in and around the focus of infection, thus enabling the tissues to get rid of a great deal of inflammatory product, and by its toning effect upon the arterioles it reestablishes circulation in the congested parts, thus restoring normal function. It therefore has a double effect: in the first place, the carrying-off of refuse products of inflammation; and in the second place the bringing of new blood supply to the

tissues, which, through the pressure of inflammatory products have been deprived of their usual nourishment.

I can only explain the diminution of septic symptoms upon the theory that by improving the local circulation the septic bacteria are carried away and destroyed more readily by the phagocytes in the blood. Whatever its mode of action, ergot certainly does accomplish results which heretofore have appeared to us unobtainable."

ERYTHROL. TETRANITRATE

Erythrol, also termed erythroglucin, phycite and erythrite, is a principle existing in many lichens and in some algae. The tetranitrate is explosive on quick heating or percussion, like nitroglycerin. It is given in the same manner and for the same purpose, that of quickly dilating the capillaries. It is slower in action and more lasting than all other members of the nitrate group. The dose is gr. 1-6 to one grain, repeated every four to six hours. It may be given in tablets. The field of this agent seems to be amply covered by sodium nitrite, whose action endures nearly as long.

EUONYMIN

Standard granule—gr. 1-67, Gm. .001; gr. 1-6, Gm. .01.

Euonymin is a resinous body derived from Euonymus atropurpureus, wahoo. By the same name is designated a crystalline glucoside whose action closely resembles that of digitalin.

Felter and Lloyd term euonymus tonic, laxative, alterative, diuretic and expectorant. It has been used successfully for intermittents, dyspepsia, torpid liver, constipation, dropsy and pulmonary affections. It stimulates the flow of bile, and is recommended for ague after quinine has broken the chills. It stimulates digestion and improves appetite. It may be used for atonic dyspepsia, indigestion from torpid liver or from malaria, for chronic malaria and the indigestion, constipation and gastric debility with or after it; for dropsy with hepatic and renal inactivity.

Specific Indications.—Prostration with irritation of the nerve centers; in periodic diseases, to supplement quinine; for anorexia, indigestion, constipation, all from hepatic torpor.

Ellingwood says euonymus is actively cathartic and alterative, through its influence on the glands. He considers it indicated in phthisis with night-sweats and great weakness, dropsies following acute affections, convalescence from severe agues, enlarged liver

and chronic bronchitis. It is a good remedy for indigestion and constipation with jaundiced conjunctiva and a yellow tint around the mouth, the tongue coated similarly; also for torpid liver and weak digestion, constipation and lithemic neuralgia. It is a hepatic stimulant, improving the protoplasmic function of the liver and increasing the bile.

Shoemaker says euonymus first increases and then lessens the excretion of uric acid. It is said to cause the disappearance of the albumin from the urine in nephritis. It also relieves that form of lumbago that is rather a soreness than actual pain.

The dose of euonymin for an adult is gr. 1 to 3, at bedtime.

Of Merck's white euonymin Van Renterghem took gr. 1-3 every hour till ten doses had been taken. Two soft stools were passed, without the least pain in the abdomen, and with no influence on the appetite or the pulse. He also tried the brown and the green euonymin, in doses up to gr. xv each. It was only on exceeding a dose of six grains that he felt, six or eight hours after taking it, a slight increase in peristalsis, followed by the usual stool. Even 15 grains did not cause laxity or colic. No effect on the pulse.

Laura ranks euonymin among the tonics and antidyspeptics, also facilitating the biliary secretion. Ruthendorf concluded that it did not act as a cholagog, but by stimulating the intestinal muscular contractions. Dujardin-Beaumetz advocated this remedy in biliary lithiasis Euonymin possesses diaphoretic properties, is a hydragog cathartic, and so we consider it antiperiodic (Ruatta). As a diaphoretic it may be associated with aconitine, for atonic dyspepsias add quassin, caffeine, or cocaine. Thibault pronounced euonymin one of the best remedies for hemorrhoids.

Laura preferred its evening administration, giving five to ten granules, each 1-67 grain, or one every hour during the afternoon. Emilio placed the medium dose at ten centigrams—gr. 1 1-2—with a range from this to .40, gr. 6. Cornil found these doses devoid of danger.

Euonymin is a cardiac tensor of the digitalis series, but this effect is subordinated to its purgative action.

Evidently euonymin is not to be looked upon as a violent drastic. Its effect seems to be in the line of correcting abnormalities in the hepatic functions. Senator praised it as a remedy for jaundice, the simple catarrhal form. In duodenal catarrh it has done well in the hands of the writer; giving gr. 1-6 every two hours, or a much larger dose at bedtime.

EUPURPURIN

Standard granule—gr. 1-6, Gm. .01.

Eupurpurin is a concentration from the Eupatorium purpureum, queen of the meadow, or gravel root.

Lloyd says this plant possesses diuretic, subastringent, stimulant, tonic and antilithic properties. It has a specific action on the kidneys, increasing both the solid and the liquid constituents of the urine. Even those who will not allow its repute of dissolving calculi admit that it controls the irritation of the bladder caused by these bodies. It has also been advised in renal dropsy, chronic mucous affections of the gastrointestinal tract, post-scarlatinal dropsy, difficult and painful micturition with frequent desire to urinate, the passage seemingly obstructed; pain and weight in the loins extending to the bladder, urine scanty and high-colored, or mixed with blood; chronic vesical irritation, a sense of heat in the bladder, urine milky and loaded with mucus, adhering to the vessel; strangury from irritant drugs or blisters, shooting urethral pains, vesical tenesmus and frequent micturition; hematuria and recent prostatitis after the acute stage passes; irritable bladder in children and in pregnancy; diabetes insipidus; vomiting of pregnancy accompanied by coughing when a little urine escapes; efficient in albuminuria; gout and rheumatism; chronic cough with weak circulation and in asthma, catarrh and unduly prolonged whooping-cough; impotence; female disorders; chronic irritability of the womb and atony; habitual abortion from prolapsus, retroversion, debility from chronic metritis, or other atonic states; as an injection in chronic amenorrhea with great debility and constant leucorrhea.

Specific Indications.—Vesical irritation, incontinence of urine, painful and frequent urination, urine scanty and milky with mucus or blood; uric acid diathesis; pain and weight in loins extending to bladder; skin dry, hot and constricted.

Ellingwood terms it specific for irritation of the bladder from displacement and chronic metritis; partial or complete suppression of urine, during or after pregnancy. He says it is also of service in chronic endometritis, insufficient labor pains, ovarian and uterine atony, dysmenorrhea, burning or dull aching in the bladder, anasarca, ague with lumbar chills, violent shaking with little sweating, severe bone pains, frontal headache, weak tired feeling, hectic with night-sweats; it increases retrograde metamorphosis and eliminates the poison causing rheumatism; acts on the ganglionic system and improves digestion.

The dose of eupurpurin is from gr. 1-6 to 1 three or four times a day. It is usually best taken in hot water, before meals and at bedtime. In the chronic maladies in which it is recommended quick results are scarcely to be expected. Give moderate doses for a month at least.

Buckley recommended eupurpurin for colicky pains and similar attacks pointing to affections of the lumbar region, and in chronic catarrhal diseases of the bladder and kidneys. He gave one or two granules every two or three hours.

GELSEMIN. GELSEMININE

Standard granules—Gelsemin, gr. 1-134, Gm. .0005; gelseminine, gr. 1-250, Gm. .00025.

Two alkaloids are derived from Gelsemium sempervirens, gelsemine and gelseminine. The first resembles strychnine in its action but is much weaker. Gelseminine is a powerful poison, resembling cicutine in most of its effects (Cushny). To the latter the effects of the crude drug are due.

Physiologic Action.—The symptoms from gelseminine are quite similar to those of cicutine, but the former depresses the central nervous system more. Death is caused by paralysis of the respiratory center. Applied locally it dilates the pupil widely, less so when taken internally. The power of accommodation is lost. But this action differs from that of atropine in that gelseminine causes paralysis of the inhibitory ganglia while atropine paralyzes the nerve terminals. Gelseminine does not increase the arterial tension but lessens it somewhat.

It is one of the most certain and powerful depressors of the motor nerves. Toxic doses cause drooping of the upper eyelids, and this is the signal for stopping the medicine. Reflex irritability is lowered, the gait is staggering, numbness is manifest, but the cerebral functions are unimpaired until carbonic acid poisoning sets in. The pulse is slowed only as the excitomotor cardiac ganglia are affected. The temperature is lowered. Great muscular weakness ensues. The arterial pressure falls.

Small doses relax the muscular system and delay nervous irritation; larger ones cause the lower jaw to droop also, and confuse the vision. The pulse slows to thirty beats per minute.

Poisoning from gelsemium calls for stimulating doses of strychnine, hot drinks and pediluvia, rubbing and other means of keeping up the heat, and artificial respiration. The stomach should be

evacuated. Atropine and morphine hypodermically are advocated by Shoemaker. Tannic acid, alkalies and their carbonates are chemical antidotes. A dram of the fluid extract has caused death.

Felter and Lloyd say that small doses relax the muscles and allay nervous irritation, causing a pleasant sense of ease; larger doses cause the lower jaw to droop as well as the eyelids; vision is confused, and still larger doses paralyze the spinal cord. Toxic symptoms are profound prostration and muscular relaxation, dropping of the under jaw and upper eyelids, dilated pupil and diplopia. The temperature falls and the pulse slows to 30 beats. Death has followed the ingestion of 12 minims of fluid extract by a child of three years. Poisoning is alleged to have occurred from the use of honey gathered from the jessamine blossoms.

Therapeutics.—The therapeutics seems obvious. Since gelseminine lessens the supply of blood to the cerebrospinal centers, it is indicated in all cases where there is hyperemia of the brain or the cord; in fact, in all cerebrospinal inflammations and hyperemias, but not in passive congestions.

Scudder gives as specific indications, the flushed face, bright eye, contracted pupil, increased heat of head, great restlessness and excitation. With these may be general headache. Such conditions arising, gelsemium will be found of use in bilious, remittent, typhoid and malarial fevers. It is best adapted to the earlier stages of fevers, sthenic forms, and is to be stopped the moment its physiologic effects are manifest, to avoid the subsequent depression. It is said that the full constitutional effect impairs the tonicity of the cardiac muscle. It is of marked value in pneumonia, pleurisy, and especially in puerperal fever. Chilly sensations on movement indicate it. Bloyer says it is specially useful for nervousness with exaggerated complaints over trifles—"touchiness." It allays excitement and restores secretion to prepare the way for quinine; in children's fevers and convulsions from dentition, gastrointestinal inflammations, cholera infantum, diarrheas and dysenteries; in hysteria, convulsions with muscular cramps, neuralgia with powerful nervous twitchings, toothache of pregnancy and of periodontitis, facial neuralgia from caries, cold or nerve excitation; insomnia, pain from nervous tension, and local hyperemia; headache from eye strain, migraine, nervous, bilious and in myalgia and tic douloureaux—give in small and rapid dosage. For ovarian neuralgia give full doses. It relieves intercostal neuralgia, sciatica, dysenteric tenesmus, bowel spasms, chorea, epilepsy, tetanus, urinary spasms, passage of renal calculi, scanty

urine with irritation of the passages; anuria from irritation not congestive; it is the remedy for dysuria from spasmodic urethral stricture, hysteric retention, gonorrhea and spermatorrhea in plethorics; in early chordee no remedy is so prompt. In spasmodic conditions with cystic catarrh, inflammations along the genitourinary tract; pelvic maladies of women, ovaritis, metritis and salpingitis, dysmenorrhea and uterine colic, rigid os uteri with dryness, it relaxes all sphincters, thus facilitates labor—give free doses. Alone or with pulsatilla it overcomes the nervous restlessness of parturients and the nervous tension following labor, as well as afterpains and some leucorrheas. By blunting peripheral sensation it relieves the itching of eczema and prurigo when applied locally. It has succeeded in delirium tremens, mania and paralysis. King used it with advantage in iritis, conjunctivitis, muscular asthenopia, and tinnitus aurium, giving small doses every four hours and carefully avoiding depressing effects.

Gastrointestinal irritation with a sense of rawness, heat and pain, or knotty contraction in the stomach, calls for gelsemium. In the exanthemata great heat and restlessness demand this remedy, and it is nearly always required in cerebrospinal meningitis. No one remedy is more frequently indicated in influenza, with persistent fever and headache, with great excitability. It has been used in whooping-cough, spasmodic cough, spasm of the glottis, asthma, hysteric cough, excessive heart action of hysterics, vertigo, hemorrhages, ague-cake, gout, rheumatism, bronchitis, laryngitis, albuminuria, and many other affections. This long list shows how great is the repute of gelsemium with the eclectics.

In their edition of King's American Dispensatory, Felter and Lloyd give as specific indications: Bright eyes, contracted pupils, flushed face, great heat and restlessness; mental irritability; insomnia with excitation; pain over the whole head; dysuria with scanty urine, irritation of the urinary tract; pinched, contracted tissues; thin, dry, unyielding os uteri with dry vaginal walls; chilly sensations on motion; hyperemia, and convulsions.

Ellingwood says the earlier successes with gelsemium were due to the full doses given. Children are more susceptible than adults to it. In spasms maximum doses are needed. Toxic effects are readily recognized and obviated without harm resulting. Gelsemium is quickly eliminated through the kidneys and the doses must be soon repeated. Single, full doses should be given only to adults. In one case evidences of poisoning came on in forty-five minutes after taking a dram of the fluid extract.

To Lloyd's list he adds: Recent torticollis, laryngismus stridulus, irritable heart-action, acute nephritis from cold, acute cystitis with great irritation and spasm; neuralgias near the head.

It is especially valuable in ovarian neuralgias, where it should be given in full doses. It gives relief in any painful or any spasmodic condition of the genitourinary apparatus. It is specific for chordee, and in the acute stages of gonorrhea in both sexes, also in acute cystitis. In fact, you learn to look upon it as almost specific in acute inflammatory or neuralgic pains in the genitourinary apparatus of either sex. It is one of our best remedies in spasmodic dysmenorrhea and uterine colic; also rigidity of the os uteri with dryness. It relaxes any spasmodic stricture.

It is a useful remedy, also, in any alcoholic delirium, in ordinary mania, and in ocular inflammations. Parrish found it beneficial in the alcohol and opium habits. It should prove especially valuable in cerebrospinal meningitis, where its particular influence seems to be exactly what we require. It promptly relieves the pains, headache and irritability of all forms of influenza, and without the depression following the use of coal-tar products. It has been praised in every form of spasmodic cough, and in all the varied affections which result from cerebral plethora.

As a rule it is best given in small doses, frequently repeated, until the desired effect is manifested. It is an especially safe remedy, since it is very rapidly eliminated; in fact, some writers say that it is difficult to obtain its beneficial effects in children for this reason, but this gives an added safety to the use of the remedy which is by no means inconsiderable. A number of writers have spoken of the value of gelseminine in breaking up recent colds.

Shoemaker says gelsemium is frequently beneficial in lumbago; might control the spasms of hydrophobia; as a substitute for morphine. Ringer found the tincture beneficial in small doses—m. x t. i. d.—in Meniere's disease. It will sometimes arrest attacks of bilious colic, in doses of m. 5 every fifteen minutes. It is of considerable service in treating hemoptysis, and a full dose may abort an acute coryza. Nottage found it useful in menopause headaches with flushes, head and body hot—gtt. 2 to 3 every three hours.

Walling took gelseminine every fifteen minutes to break up a cold. Four doses did the work and induced dizziness. Another patient took six granules with like success; but the patient said the medicine made him drunk. These doses were gr. 1-134 each, and they were evidently too strong. Reducing to gr. 1-250, no further trouble was experienced.

Dr. M. G. Price of Mosheim, Tenn., cured a case of neuralgia with gelseminine after the galenic preparations of the same drug had proved worthless. In influenza Barnes gives gelsemium with strychnine for the fever, aches and pains, cough and restlessness. He credits it with a special action on the ophthalmic division of the fifth nerve.

This long list by no means exhausts all of the maladies for which gelseminine has been recommended. Every use, however, which has been suggested by the remedy is fully sanctioned by a study of its physiologic action.

The dose of gelseminine ordinarily employed for an adult is 1-250 grain, and this may be repeated every ten, fifteen, or thirty minutes as the occasion requires, until drooping of the eyelids and weakness of the lower jaw indicate a full and beginning toxic action of the drug, when it is to be discontinued or repeated less frequently. Thus given it is absolutely safe and of its efficiency no one who has given it a trial has any shadow of a doubt. Before this sign appears, dryness of the mouth denotes the full therapeutic effect.

Sollmann states that the depressing action of gelseminine on the central nervous system is more marked than that of cicutine, although in general the effects of the two are almost identical. The mydriasis of gelseminine lasts twelve to seventeen hours.

Dumas says that in gelseminine we have a valuable addition to our armamentarium of treating yellow fever. Probably its sedative effect on the nervous system, and its antimalarial properties, account for the benefit secured.

The virtues of gelsemium are fully represented by gelseminine, and this alone should be used, the concentration gelsemin being dropped, and the galenic preparations also, for their uncertainty. The dose of gelseminine is gr. 1-250 repeated every quarter-hour in acute cases and every two hours in chronic ones.

We have frequently expressed our conviction that when these remedies have been thoroughly studied, it will be found that they possess certain variations in action, which correspond to variations in the clinical phenomena presented by disease; which will render each of these remedies applicable in certain conditions rather than the others. Unfortunately, in the general neglect of therapeutics which has prevailed during the last few decades, the profession has contented itself with accepting strychnine as representative of the group, and neglecting all the others. Nevertheless, strychnine stands at the head of the materia medica today as the most universally-relied-upon agent now in use as a strengthening remedy.

Gelsemium usually depends upon gelseminine for its effect, this being present in quantities that overbalance the gelsemine. This is by no means certain to be the case, however, and in some conditions we may have an almost pure strychnine effect from the crude drug. At any rate gelsemine may be present in any specimen in sufficient quantity to notably influence the action of the drug. Hence, for accurate therapeusis, as well as for scientific study, it is necessary that we should avail ourselves of the alkaloid when extracted and separated.

A physician more than fifty years old had suffered for some time with cystitis and excessive irritability of the bladder, largely dependent upon a urethral stricture, which he would not allow to be touched. He was taking about six grains of morphine daily, had been for about four years; even this failed to give him complete relief and every night he was awakened by the necessity of emptying his bladder seven or eight times, while he could not go far from his home at any time during the day on account of this necessity. As the morphine was discontinued, he developed a rather tense pulse and naturally an increasing irritability of the bladder, with two degrees of fever, a flushed face, bright eye, and quite marked fulness of the cerebral vessels.

Altogether, the picture presented was that of the indications for gelseminine, since these seemed to meet all the features of the case, including the irritability of the bladder. I therefore one evening substituted for his evening dose of morphine, 1-50 grain of gelseminine hydrochloride, given hypodermically. The patient rested through the whole night, only rising twice to urinate, and did not call for morphine during the night. When he asked for his morning dose of morphine, the next morning, he received instead the same dose of gelseminine, and from that time on he received no more morphine, but only gelseminine, the latter giving complete relief, in fact, so complete that the patient never knew but what he was taking morphine. One peculiarity about this is that at night, a single dose at bedtime seemed to give him complete relief until morning, even though he did not sleep the entire night, but awoke several times. During the day he would call for a dose every two to three hours. He took as much as six or seven doses during the twelve hours that he was up, without causing at any time any marked toxic symptoms; he really seemed to tolerate gelseminine to a remarkable degree.

The result was very satisfactory in one or two other cases, where there were no bladder complications, but slight fever and

slight fulness of the head with the restlessness always seen when patients discontinue their accustomed morphine. I administered the same dose of gelseminine hydrochloride hypodermically and with the happiest results.

Although experience has taught me that one, two or three cases do not suffice to form a rule, I must say that the relief following the use of gelseminine has very strongly impressed me; and I shall certainly give further trials of this remedy along this line. However, I do not expect to find gelseminine a cure for the morphine habit, nor to find it very extensively applicable. I believe it will prove like pilocarpine, physostigmine and a number of other remedies—it will give relief when it is indicated and not otherwise.

Synergists.—Macrotin when the muscles are affected, heart and genitourinary cases; passiflora, bromides, chloral, cicutine, physostigmine, veratrine. Antagonists are alcohol, strychnine, digitalin, ammonia, and to some extent atropine and caffeine. Coffee is an antidote.

GERANIN

Standard granule—gr. 1-6, Gm. .01.

Geranin is a concentration from the rhizome of Geranium maculatum. The active principle is tannic acid, which in the dried root changes to gallic acid. The yield varies from 28 percent in spring to 10 percent if gathered in October. The virtues of geranium are those of the vegetable astringents. Whether there is any advantage in using the crude plant preparations instead of pure tannic acid each physician will decide for himself.

Therapeutics.—As an astringent geranin may be employed in the relaxed stages of diarrheas, dysenteries, choleraic affections, and locally for hemorrhages, ulcers, aphthae, ophthalmia, gleet, leucorrhea, salivation, and any place where an astringent is indicated. It has also been given internally for diabetes, menorrhagia, hematuria and chronic mucous discharges of all kinds. In chronic pharyngeal catarrh it has been employed as a gargle; and it has been advised even as a remedy for incipient tuberculosis. King recommends it with aletris for diabetes and nephritis. It is applied to bleeding hemorrhoids, epistaxis, bleeding from small wounds and from tooth cavities, etc. King wisely advises the addition of berberine in most of the cases enumerated above. Like other of the tannin astringents geranin is advised as pleasanter and less irritant than the acid itself, and this may be true. But the use of tannic

acid in granules leaves little to be desired when a vegetable astringent is indicated.

GLONOIN

Standard granule—gr. 1-250, Gm. .0025.

Glonoin is the one remedy whose effects are more quickly manifested when taken by the mouth than when administered hypodermically. Within a minute after taking a dose the patient feels a sense of fulness in the head with throbbing, and the face and neck flush. Darwin pointed out that the area affected corresponds exactly with that of ordinary blushing. Brief headache follows, and a sense of impending dissolution if the dose has been too large. If very large doses are taken there is vertigo, prostration, and stupor. The respiration is rapid and irregular, but shallow. Within five minutes these effects pass off, and leave the patient none the worse. There is an instant and profound fall in the vascular pressure, due to dilatation of the arterioles and veins of the surfaces of the body. The pulse is faster. The dilatation of the vessels is believed to be due to a direct action on the muscular fibers of the vessels. The rapid pulse is due to depression of the inhibitory center in the medulla. Large doses directly weaken and slow the heart. The faster breathing is due to a direct action on the respiratory center in the medulla. With lethal doses the respiration becomes shallower and death occurs from paralysis of this center. The urine is slightly increased, especially if the renal vessels are contracted, as in cirrhosis; but if normal there is a decrease in the urine from relaxation of the pressure in the renal artery. No effect is exerted on the higher cerebral centers except indirectly through the dilatation of their vessels. Some anomalies of sight follow large doses. Convulsions may follow toxic doses. The temperature is lowered to an unimportant extent. The blood may be darkened by the formation of methemoglobin.

Glonoin is partly decomposed in the blood, and partly excreted by the kidneys.

So far Cushny conducts us. Shoemaker says glonoin lessens reflex excitability, retards oxidation, and in large doses stops the heart in diastole.

Sollmann sums the action of the nitrites as paralysis of the vasoconstrictor mechanism, mainly peripheral; of the vagus center; slow paralysis of all muscle fiber with which they come in contact; and methemoglobin formation. With erythrol nitrate the effects appear only after fifty minutes and last five hours.

A. T. Cuzner warmly advocates glonoin in labor cases that require a uterine stimulant.

Therapeutics.—Brunton introduced the nitrites as remedies for angina pectoris, in which they speedily give relief by relaxing spasm of the arteries and the vascular tension. The instantaneous relief from agonizing pain and imminent danger forms one of the most striking exhibitions of therapeutic power known. In other spasmodic affections this remedy acts equally well; and it has earned the designation of "the life-saver." The paroxysm of spasmodic asthma relaxes at once after a few granules of glonoin. In the case of renal or hepatic colic, due to the passage of calculi, a granule of glonoin is administered with one each of atropine and strychnine arsenate, to open the blood-vessels and permit a speedier action of the more enduring remedies. The pain is relieved quickly by glonoin and this effect is prolonged by atropine. In many cases glonoin is given to hasten the action of other remedies.

In cirrhotic nephritis, when the pulse is tense and small, the heart hypertrophied, glonoin has been given with the best results, to relax tension and obviate the dangers arising from this condition. Here there has been observed a toleration of the drug, until in one instance the incredible dose of six grains has been recorded. However, as this is a remedy whose effects are evanescent it seems better to use it for quick effect and to rely upon veratrine to keep up a continuous depression and relaxation of the circulation.

On the heart the effect needs to be carefully studied, that the benefits of this invaluable remedy may be secured without its dangers. By sending the blood quickly to the head it at once stops fainting or syncopal attacks; but the drop in vascular tension may be perilous. It is better to give glonoin with brucine which acts quickly enough to counteract the subsequent depression. In obstructive diseases of the heart, small doses of glonoin relieve the weak organ by relaxing arterial tension, and thus making the work easier. But as the effect is over in a few minutes this use of glonoin is much overrated. Nor when given with digitalin can glonoin be relied upon to counteract the increase of vascular tension caused by this powerful drug; as in the combination of glonoin, digitalis, strophanthus and belladonna; whose effects endure for days. This prescription, attributed to Da Costa, never came from that great therapeutist. Here also veratrine would accomplish the indication far better.

It has been advised to add the allied agent amyl nitrite to chloroform when used for inhalation, as the former counteracts the

tendency to cerebral anemia; but the same objections hold good, and the result can not fail to be an increase of the danger.

Headache due to cerebral anemia is relieved momentarily by glonoin but much better by atropine.

Lanphear recommends glonoin for shock after operation presenting imminent danger. If the shock is purely of nervous origin benefit will be noticed very soon. If not, a second dose may be given in ten minutes, but not a third.

The headache following inhalation of the gases liberated by the explosion of nitroglycerin powders is relieved by coffee and by counterirritation to the neck; better by inhaling iodoform.

In the first stage of an epileptic convulsion the condition is a cerebral anemia, and this may be instantly removed and the convulsion aborted by glonoin. Add atropine to prolong the effect, and we have a remedy whose efficiency the writer has proved in many cases. Sometimes the convulsive tendency is too strong to be permanently postponed in this way, but in others the patient has kept the fits away for months by resorting to the remedy whenever the impulse to a spasm is felt. Time is given for etiologic treatment, while the striking effects of the glonoin aid in breaking up the habit.

Glonoin has been advised to relieve the craving of the habitué for opiates; as a remedy for morphine poisoning; in Raynaud's disease—where also the writer has used it with benefit and substituted veratrine with much more—and for poisoning from illuminating gas.

Shoemaker cautions against tablets of too great strength as liable to explode.

In the form of "sunstroke," that is really heat exhaustion, with relaxation, feeble pulse and syncope, the best treatment is by glonoin, atropine and brucine, administered intensively.

Ellingwood says glonoin has controlled many cases of postpartum hemorrhage. He speaks of giving it hypodermically in cases of drowning, gas poisoning, and opium poisoning with uremic symptoms; it has caused relaxation in tetanus; and in pallor with palpitation.

Bartholow recommended glonoin to ward off the chill of ague.

Dr. M. G. Price, of Mosheim, Tenn., finds glonoin very effective in gastralgia of adults and of children; in eclampsia with high tension this is abated by it; in dangerous collapse and syncope this is the remedy above all.

Abbott says glonoin relieves congestion. He advises it in high temperatures with pale skin.

Dr. S. J. Smith with glonoin saved the life of a man who was poisoned by aconite.

Dr. A. H. R. Ginley gave glonoin to a child with cyanosis neonatorum for two weeks, finally saving its life.

Dr. D. S. Ross reports the case of a man 84 years old, unconscious from the onset of pneumonia. He regained consciousness with glonoin and recovered. But it is always wise to add agents more sustained in action, like brucine.

Dr. J. F. Brenckle reports the case of a woman two weeks over confinement, seized with gastralgia and dyspnea, with weak rapid pulse. She was almost immediately relieved by glonoin and strychnine and digitalin. Pericarditis with effusion was present.

Dr. R. V. Pearce records what was really a case of glonoin habit, the patient taking it under the mistaken idea that it was necessary as a heart tonic.

Dr. E. H. Winkler, of Arkansas, speaks highly of glonoin as a remedy in asphyxia neonatorum. He applied the solution to the child's tongue. Even when no heart-beat can be detected, if there is a spark of life the effect is often instantaneous. Several doses may be required.

Dr. W. O. Hamilton used glonoin in an infant with opium poisoning, with success, when amyl nitrite had failed; also in asphyxia from hypertrophied tonsils, malarial chills, emphysema, and in syncope with hourglass contraction in abortion.

Glonoin is warmly recommended by Hugh M. Moore, of Ohio, in the treatment of dysmenorrhea. He commences the use of this agent during the week preceding the expected menstruation. When the flow begins 1-100 grain of glonoin is administered every three to five hours according to the effect, the blood tension being the guide. During the first few periods small doses of morphine, gr. 1-16 each, are given to control the pain. This is discontinued as soon as the flow is established and the pain ceases. Glonoin regulates the vascular pressure, quiets the sensory nerves, increases the trophic changes in the muscle fibers and stimulates glandular activity.

The granules of glonoin are too strong. Many persons like the writer cannot take gr. 1-250 without disagreeable effects. A dose of gr. 1-500 would be preferable. This should be given every five minutes, or several granules at once—always crushed by the teeth—in emergencies. Flushing of the face and a sense of fulness of the head, are indications of full therapeutic effect, when the remedy should be suspended.

GOLD

Standard granules—Gold bromide, gr. 1-67, Gm. .001; gold chloride, gr. 1-67, Gm. .001; gold and sodium chloride, gr. 1-50; gold and sodium chloride, gr. 1-20.

The effects of gold closely resemble those of mercury. The action is slower in being produced when given in medicinal doses but the effects are more lasting. In a case of salivation from gold the writer was months in getting the affection under control.

Gold has bactericidal powers even superior to those of mercury. Especially are these shown against the tubercle bacillus (Shurley and Gibbes). It increases the secretions and excretions in general, as does mercury, and stimulates metabolism. The vital processes are quickened universally, the red cells and hemoglobin increased, and a rise of temperature is caused. Like corrosive sublimate the salts of gold are corrosive when concentrated, and cause vomiting, diarrhea, and other evidences of gastrointestinal irritation. The urine is increased, and too large doses cause renal hyperemia and albuminuria. The property of increasing the sexual appetite and powers in both sexes has been attributed to gold, but if true this effect is pathologic. Here too the effect parallels that of mercury.

Gold is eliminated by the kidneys, the liver and the bowels.

Therapeutics.—Gold bromide has been tried largely as a substitute for the big-dose bromides in epilepsy. There is a bromide effect obtained from the gold that is truly remarkable when one considers the minute quantity of bromine in it; but it is better as an adjuvant than a substitute. Give sodium bromide till evidences of bromism appear, then add the bromides of gold, arsenic and nickel successively, and excellent results are obtained. Care must be had in pushing this remedy to toleration, as its salivation is not indicated by tender teeth as with mercury. Auric fever and gastric disorders are caused by overdoses. Thus employed, the bromide treatment is a valuable auxiliary to the hygienic methods indicated in this disease.

Shoemaker credits gold with a valuable action in atonic dyspepsia, nervous dyspepsia, gastric catarrh, torpid liver, etc.; but in all these there is no evidence to show any advantage over mercury, which is cheaper, easier to obtain and to handle. In the early stages of cirrhosis gold has been given with asserted advantage. As cirrhosis means a destruction of gland cells and replacing them with connective tissue, it cannot be supposed that any remedy can renew the lost tissue. But if there is enough gland tissue remaining to keep the patient alive today, it should suffice for tomorrow; if

only the cirrhotic process may be stayed. And possibly gold may contribute to this end. At any rate it has been largely given in cirrhosis of the liver and of the kidney, with asserted advantage; and Culbertson reported relief of albuminuric retinitis from this remedy.

Gold has been used for arteriosclerosis, the vertigo of the aged dependent thereon, and for vertigo due to indigestion. The iodide of arsenic has proved very useful in these cases and the iodide of gold may be still better.

Gold has been advocated in whooping-cough, laryngismus stridulus, hysteria and functional impotence. It is useful in amenorrhea and dysmenorrhea due to deficient innervation, and as a preventive of abortion, as mercury is in similar cases. From the physiologic action Shoemaker deduces its value in spinal sclerosis, premature senility, depression and hypochondria, neurasthenia, progressive general paralysis, uteroovarian congestion, menorrhagia, subacute metritis, nymphomania and spermatorrhea. Better based is Strahan's recommendation of this metal in cerebral anemia.

Sometimes syphilitics cannot bear mercury and gold will take its place. We believe the effects are rather more enduring, but it is only in exceptional cases that the more costly metal is indicated. It is usually given in tertiary forms of syphilis.

Robinson found that gold cured two cases of diabetes mellitus; and many subsequent cures have been claimed from various salts of this metal.

Lydston reported success in treating pyelitis with gold administered hypodermically.

Calmette says the venom of the cobra may be antidoted by injecting a one-percent solution of gold chloride, 2 to 2 1-2 drams, into and about the wound, not more than 15 minims at one spot. The solution may be thrown into the connective or the muscular tissue. Injections are also made at the ligature about the limb, and above it. When this has been done, the ligature may be removed.

Shurley and Gibbes reported remarkable success in treating tubercular phthisis with hypodermics of gold and sodium chloride, gr. 1-20 to 1-6 daily, for several months.

Reviewing the evidence in regard to gold, we are unable to find positive proof of its utility in any malady except syphilis; though it may be useful, and is surely deserving of trial, in tuberculosis, cirrhosis, and when injected locally in cancer and lupus.

The dose of any of the auric salts is the same as of corrosive sublimate—gr. 1-67 to 1-6 up to the appearance of evidences of approaching salivation.

GOSSYPIN

Standard granule—gr. 1-6, Gm. .01.

Gossypin is a concentration from the bark of the cotton root, Gossypium herbaceum. The virtues appear to reside in an acid resin.

Cotton root is an emmenagog, and was used by southern slaves as an abortifacient. It has the repute of acting much less acridly than ergot and without much general disturbance. Felter and Lloyd recommend it in uterine inertia, chlorosis with amenorrhea or dysmenorrhea, etc. It has been praised in hysteria, anemia of the sexual apparatus with lack of desire and pleasure; also for impotence, subinvolution and uterine fibroids, but is not to be used if there is irritation or tendency to inflammation. It is a stimulant diuretic.

Specific Indications.—Uterine inertia during parturition; menses delayed with backache and dragging pelvic pain; fulness and weight in bladder, with difficult micturition; hysteria with anemia of genitals, sexual lassitude.

Ellingwood pronounces gossypium of value in suppression of the menses from whatever cause; producing firm, regular and strong uterine contractions. It is a hemostatic of some power, for uterine fibroids and incipient cancer; valuable in menorrhagia and metrorrhagia.

Phillips found cotton root useful in hemoptysis. It has been used in the West Indies for dysentery, and Poteyenke employed it as a general hemostatic, especially in a peculiar epistaxis which had resisted other remedies.

The writer's uses of gossypium have been disappointing. Possibly the fresh plant contains virtues not present in the preparations of the pharmacy.

GREGORY'S SALT

Standard granule—gr. 1-67, Gm. .001.

Gregory, of Edinburgh, gave a process for the extraction of morphine, which consisted in precipitating by calcium chloride, a concentrated solution of opium; an insoluble meconate of lime formed, and the chlorate of morphine remained in solution; which

was crystallized by concentration. Robiquet found that the product did not correspond with the chlorate as indicated by reaction, and suspecting that the salt was impure, he isolated the morphine by means of ammonia, and obtained with potassa a new precipitate, soluble in ether and crystallizing admirably in presence of water. This proved to be codeine, and the salt procured by Gregory a mixture of the chlorates of morphine and of codeine.

This salt has been used by the French dosimetrists to some extent, and is preferred to morphine. In America codeine itself has largely replaced morphine as a remedy for coughs, and there seems little place for Gregory's salt. Possibly it may answer to throw some too wise patient off the track, as the older physicians were accustomed to do when they prescribed Aquila alba, or Panchymagogus quercetanus for calomel. Gregory's salt is about half the strength of morphine, but is obviously subject to the variability of opium itself, as to the relative proportions and actual amount present of each.

GUARANINE

Standard granule—gr. 1-67, Gm. .001.

Guaranine is an alkaloid obtained from the Paullinia sorbilis, a plant found in Brazil. The alkaloid is practically identical with caffeine, containing a small proportion of theobromine in addition. The action and therapeutic applications are the same as with caffeine, and to detail them here would be a useless repetition. The presence of theobromine may render guaranine slightly more diuretic.

HAMAMELIN

Standard granule—gr. 1-6, Gm. .01.

Hamamelin is a concentration from Hamamelis Virginiana, the witch-hazel. No glucoside or alkaloid has been obtained from hamamelis, which contains tannic and gallic acid, and a volatile oil.

Felter and Lloyd term witch-hazel tonic and astringent. They speak of its use in hemorrhages, diarrhea, dysentery, excessive mucous discharges with full, pale relaxed tissues; in incipient phthisis; as a local application for painful swellings and tumors, sore mouth, external inflammations, prolapsus ani and uteri, leucorrhea, gleet and ophthalmia. Its most pronounced virtue is in affections of the veins, its tonic action being markedly shown

in varicosities, hemorrhoids and hemorrhages. The parts are usually pale and relaxed, though sometimes the deep red of venous engorgement is seen. It is adapted to the whole venous system.

Scudder and others have found it a valuable remedy in passive hemorrhages and congestions, epistaxis, hemorrhoids, phlegmasia dolens after the acute phases, phlebitis and varicose veins; diarrhea, chronic pharyngitis, chronic uterine congestion when the cervix is enlarged without abnormal hardness, the os soft, open, with leucorrhea and prolapsus possibly; diarrhea with passive hemorrhage; chronic vascular conditions of mucous tissues, and old flabby ulcers.

Howe gave hamamelis in uterine hemorrhages with success; in menorrhagia and bleeding after abortion no other remedy did as well; in post partum cases it was not equal to ergot; it was valuable in chronic diarrhea and in cholera infantum; arrested oozing of blood from mucosa, and in non-inflammatory hematuria. It is often of value in renal affections due chiefly to vascular relaxation; diabetes insipidus, mucous profluvia of the urinary tract, vesical catarrh, and irritation of the bladder from varicocele. In female disorders it is indicated by venous fulness and relaxation; dull aching ovarian pains; leucorrhea with fulness of the pelvic veins and relaxation of the utero-vaginal walls; ovarian and testicular congestion; ocular and conjunctival hemorrhages; sprains, contusions, wounds, with asepsin as a dressing for small wounds; with hydrastis for irritation of the external auditory meatus; chafing; diffuse cutaneous inflammation; subacute sore throat; scarlatinal angina; tonsillitis, phlegmon of throat, diphtheria, acute pharyngitis, chronic conjunctivitis with vascular lids; mastitis; soreness of abdominal muscles after childbirth; muscular soreness and aching from any cause; tan, freckles, sunburn, dilated facial capillaries; as a wash after shaving; an injection for gonorrhea; an ointment for piles.

Specific Indications.—Venous debility with relaxation and fulness; pale mucosa—or deep red or blue from venous engorgement or stasis—mucous flow with venous fulness; passive hemorrhages, varicoses, capillary stases, hemorrhoids with sense of fulness; relaxed and sore throat; dull ache in rectum, pelvis or female genitals; perineal relaxation with fulness; muscular relaxation, soreness, aching or bruised feeling from cold, exposure, injury, strain or physical exertion.

Ellingwood says hamamelis is useful for bleeding from a tooth cavity, from the posterior nares, or from spongy gums; quickly cures acute hemorrhoids and with collinsonia greatly benefits chronic cases; and gives prompt relief to burns and scalds.

In all cases where possible this remedy should be given internally and applied locally at the same time. The specific virtues probably reside in the volatile oil, and are lost in the galenic preparations, which owe whatever value they may possess to the tannic acid present. As to the indications—the whole story is told in the two words: Relaxed veins.

Hamamelin may be given in doses of gr. 1-6 to 2 every hour or two.

HELENIN

Standard granules—gr. 1-67, Gm. .001; gr. 1-6, Gm. .01.

The introduction of alkaloidal medication will undoubtedly result in the rescue of some remedies formerly prized, but which have fallen into disuse from the uncertainty attending the old preparations.

Ever since Germain Sée demonstrated the great advantage which accrues from the uses of medicaments that are simple, crystallized, of definite composition, whose action when seriously studied and carefully determined proves to be always the same, many new medicaments have been discovered and extolled. A great number of them, it is true, have been in vogue but ephemerally, yet some of them have taken solid root and have preciously enriched our pharmaceutic arsenal, among which is counted helenin, which occupies an important place because its therapeutic value is incontestable.

Alant-camphor (helenin) is a yellow, hard mass, obtained by steam distillation from the root of Inula helenium. Recent investigations prove this substance to be a mixture of a fluid and a crystallizable substance, which can be separated by pressing between blotting paper.

Helenin is the name given also to a stearopten, obtained as a by-product with alantol by mixing water with the alcoholic extract of the root, and repeated recrystallization of the precipitate. This forms large, colorless, loose, bulky needles, melting at 231.2° F., almost insoluble in water, easily soluble in alcohol, ether and oils. It is not volatile unless decomposed. It does not form salts with acids or alkalies but is decomposed by them.

Physiologic Action.—In doses of Gram 0.01—0.05 many times daily, in health, helenin produces no notable effect. One part suffices to prevent putrid decomposition in 10,000 parts of urine (Korab). The local application if too long continued causes erythema.

This agent acts primarily on the mucosa, especially of the respiratory organs, on the lymphatics and the glands. It renews the functional activity of these organs and gives new energy to the tissues, as shown by improved secretions. Having entered the fluids it favors vegetative metamorphosis, liquefying and dissipating exudates—a quality that explains its curative action in specific dyscrasias (Van Renterghem).

Therapeutics.—It is a stimulant to the digestive organs, the circulation and the principal secretions. Larger doses cause nausea and vomiting. It is then a tonic aromatic, with expectorant, diuretic and diaphoretic properties. This remedy may be utilized in atonic dyspepsia, general debility, torpid dysmenorrhea, pulmonary and bronchial catarrhs, exanthematic fevers with retarded eruptions, and even in the depression following the introduction of a poison or venom (Gubler). Elecampane was one of the ancient remedies for venomous bites, and highly prized.

Huesemann speaks of the local use of helenin for pruritus.

Knakstedt pronounced it very efficacious against eczema and other skin affections, especially scabies, for which it should be applied locally and taken internally.

Valenzuela, Korab, Blocq and others, publish accounts that seem little short of miraculous, of the effects of helenin on respiratory maladies, and as an antiseptic in dressing wounds. In tuberculous and other forms of pulmonary phthisis, chronic bronchopneumonia and whooping-cough, it gave good results. One chronic bronchopneumonic, aged 46, had for eight months resisted all treatment. He was given helenin, gr. v—x daily, and was cured in fifteen days. A consumptive, aged 36, with tuberculous foci in both lungs, hemoptysis, etc., took helenin Gram 0.01 ten times a day for two weeks, with rapid improvement, and both lungs became permeable. In all cases improvement resulted. In chronic bronchitis the cure nearly always proved complete.

In whooping-cough the efficacy of helenin is termed marvelous, every case resulting in a surprisingly rapid cure. The drug was given internally. Simultaneous inhalations of helenin gave no advantage. The cough always remitted, as well as the dyspnea and thoracic pains, all ceasing completely, without the least sign of narcotism. The sputa lessened and became gelatinous, an effect so special that it could not fail to attract attention.

On the digestive tract helenin exerts a very marked tonic action, increasing appetite and aiding digestion, even in phthisics with unconquerable anorexia.

One of the most remarkable properties of helenin is a notable reduction of laryngopharyngeal excitability. (*Soc. de Biol.*, May 13, 1882.) Helenin is therefore one of the best medicaments for quieting cough; it will stop the most rebellious cough paroxysm, dry up expectorations the most abundant, and palliate much asthmatic dyspnea. When ingested it exercises a high degree of stimulating action accompanied by a marked diminution of vascular tension and a lowering of temperature, phenomena which were rigorously studied by means of Prof. Marey's apparatus. (*Soc. de Biol.*) From these physiologic properties it was readily deduced that it would be useful in the treatment of pulmonary congestions and to prevent hemoptysis, and these effects have been well demonstrated in clinical experience. Helenin acts remarkably against pulmonary congestions, and its effects are useful also in cases of ulceration and even in cavernous cases when the purulent breath of broken-down tissues (in phthisis) makes us fear the rupture of some blood vessel which has become too thin to resist the pressure of the blood current.

Helenin affords the further advantage of being ingested without irritating the stomach. It stimulates the appetite like the aromatic bitters, and is an aid to digestion in phthisical patients who suffer from obstinate anorexia.

As a powerful microbicide this body has a sterilizing action on Koch's bacillus (Acad. des Sciences, Sept. 4, 1882). De Korab proved this as early as 1882, and in 1885 Pillatte verified it and in a Montpellier thesis remarked that a minimum quantity of helenin sufficed to hinder the development of the bacillus.

We must not forget also that helenin is eliminated very rapidly by way of the respiratory passages and it is this fact that explains its topical action on the bronchial mucosa and pulmonary parenchyma (Congress Internationale de Therapeutique, 1899).

Summing up the above we would say that the properties of helenin fully justify the opinion put forth by the distinguished clinician, Vindevogel, in an article of his in the *Confraternite Medicale Belge*, where he says that we are to congratulate ourselves on the introduction of helenin in modern therapeutics.

Commenting on these glowing accounts, Van Renterghem describes the case of a lady, who had chronic laryngitis with acute exacerbations. She improved under other treatment but the hoarseness persisted, with incessant cough. He gave her helenin Gram 0.01 every hour. By the second day she had improved, and a cure resulted within two weeks.

In another case of spasmodic asthma, chloro-anemia and bronchitis, with evening fever, cough, debility, green purulent sputa and anorexia, helenin was given, Gram 0.01 every hour; with strychnine 0.0005, quassin 0.001, sodium arsenate 0.001, four granules each before meals; and daturine a granule every half-hour till effect, to cut the asthmatic attack. The treatment was crowned with success, all symptoms disappearing within three weeks.

Helenin is a remedy with a future. Its special action on the respiratory mucosa suggests its elimination by the lungs. The inefficiency of the inhalation of helenin shows that, like arbutin, it is transformed in the body. Though not a specific for all pulmonary maladies, helenin is still a very valuable acquisition, in all forms of chronic bronchitis, simple or diathetic; in chronic lobular pneumonia and in whooping-cough. This list may be extended by further essays of the remedy.

Merck says alantol is an internal antiseptic and anticatarrhal; used in pulmonary tuberculosis instead of turpentine. Dose Gram 0.01, t. i. d.

As helenin does not exert any evident action in health no indication of physiologic effect can be given. The usual dose is Gram 0.01 (gr. 1-6) every one to two waking hours. Elecampane formerly had a reputation as a remedy for snake bites and other poisonous wounds, but no recent essay of its virtues has been recorded.

HELONIN

Standard granule—gr. 1-6, Gm. .01.

Helonin is a concentration from Helonias dioica.

This plant contains a neutral principle soluble in alcohol and water, whose properties have not yet been studied, further than that it is said to act as a "heart poison."

The American Dispensatory gives the following information:

Helonias is tonic, diuretic, and vermifuge, in large doses emetic and when fresh sialagog. It has proved useful in dyspepsia, anorexia, and to remove worms; indigestion, and malassimilation due to disease or reflex from the female genitals; chlorosis from the same cause; the gastric symptoms of nephritis; colic, genital atony, nocturnal emissions from excess, with impaired memory and apathy; general weakness and dull renal or lumbosacral pain; as a uterine tonic in amenorrhea, dysmenorrhea, leucorrhea and to remove the tendency to repeated miscarriages; it relieves the irritability and despondency attending uterine disease; dysmenor-

rhea with pelvic distention, the womb feeling as if ready to fall out of the body and aching (best here in small doses); vomiting of pregnancy; diabetes insipidus; distinctively a uterine tonic.

Specific Indications.—Mental irritability and despondency, sexual lassitude, atony of female reproductive organs; gastric debility, anorexia, nausea, indigestion and malassimilation when due to uterine reflexes; sticky, slimy leucorrhea, atony of urinary tract, dysmenorrhea with pelvic fulness and heaviness, bearing down as if parts would fall out.

Ellingwood pronounces it a liver remedy of rare value; useful for dragging and weight in the male bladder; it quickly overcomes phosphaturia and is useful in nephritis.

It is to be regretted that the members of this valuable group of vegetable uterine tonics have only been presented to the profession in mixtures and combinations, so that the specific virtues of helonin, aletrin, mitchellia, dioviburnin, senecin, and others have not been made out. The only attempt at such a differentiation yet made is by the eclectics; and as this is directly in line with our efforts at accurate medication, we have given the specific directions for the uses of each of these remedies as laid down by the leaders of this school. Follow these until your own observations have given you a better guide.

The dose of helonin is gr. 1-6 every half-hour in most cases; gr. 2 four times a day when smaller doses fail.

HYDRASTINE

Standard granules—Hydrastin, gr. 1-6, Gm. .01; hydrastine, gr. 1-67, Gm. .001.

Hydrastin is a concentration from Hydrastis Canadensis, and contains the combined alkaloids, hydrastine, berberine and canadine.

Kehrer, after elaborate experiments, comes to the following conclusions: (1) Automatic contractions of uterine muscles are benefited by hydrastis and ergot, even though the uterine nerves are severed. (2) Extract of hydrastis has the least action of all of the hydrastis preparations, hydrastine and hydrastinine being much stronger. (3) Styptol and stypticin have a stronger action under the same circumstances. (4) Hydrastine, hydrastinine, styptol and stypticin have a susceptible action in dilution of one in two hundred thousand, and therefore have about the same value. (5) This action occurs in all stages of development of the uterine muscles,

from birth through all stages of pregnancy. (6) Berberine has no action on the uterus. (7) With intravenous, intramuscular or subcutaneous injection of these, the action is similar to that described. No sedation could be determined for any ergot preparation. (8) All these cause temporary cardiac depression followed by a moderate increase in blood-pressure, due to action directly on the blood-vessels. (9) Uterine muscular contraction follows the tendency of blood-vessel contraction. (10) The complete resemblance between ergot, hydrastis and cotarnine speaks against the use of the last two in hemorrhage during pregnancy.

Canadine resembles morphine in action but is present in too small proportion to markedly influence the effect.

Hydrastine exerts a slight local anesthetic action. While large doses cause a decided fall of vascular pressure, the action of small doses is uncertain—probably because of the variable specimens with which experiments were made. Marfori says it seems only safe to conclude that the rise of blood pressure is uncertain, usually small and short, and soon followed by a fall due to vasodilatation and depression of the heart. It is evident that the vasoconstriction is a small-dose effect strictly.

Hydrastine is sparingly soluble in water, unless acidulated; soluble in alcohol, ether and chloroform. Large doses slow the pulse and still larger ones cause weakness, tremors, dyspnea and incoordination. Very large doses induce clonic and then tonic convulsions and tetanus, during which respiration ceases (Cushny). The pulse slows at first from stimulation of the vagus center, then quickens as it is paralyzed, and later again slows from a direct action on the heart muscle. The vascular pressure rises from contraction of the arterioles, then falls from their relaxation and the weakening of the heart. The vasomotor center in the medulla is directly stimulated. Cushny questions the asserted action of hydrastine upon the uterine-fibers, and that upon the liver. The respiration is at first faster. Besides its action on the centers hydrastine weakens and paralyzes the muscular fiber of the heart. This effect resembles that of thebaine. Hydrastine is excreted by the kidneys. A cumulative action has been observed. Death from lethal doses is due to heart paralysis.

Some diuretic action is exerted.

Therapeutics.—Hydrastin has long been used as a bitter tonic. It is an astringent, gradually reducing redundant secretions. It has been employed as an injection in gonorrhea, vaginitis and leucorrhea, and given internally. For various forms of stomatitis,

syphilitic, mercurial and digestive, it is an efficient lotion. Many other applications of this valuable astringent are made, such as a lotion to ulcers, fissured nipples, otorrhea, pharyngitis, and any skin disease with secretion to be checked. Shoemaker recommended it in ointments in bromidrosis, carcinoma, etc.

Unhealthy ulcers, chancroids and sloughing sores are benefited by this application. Internally hydrastin has been used with benefit in gastric and duodenal catarrhs, especially those of drunkards, their morning vomiting, jaundice and enteritis, all of the chronic type. It checks the loss of albumin in desquamative nephritis. As a hemostatic it has succeeded when ergot failed; in bleeding piles, hemoptysis—where Marini pronounced it the best hemostatic—and for the hemorrhage of uterine fibromas.

As an oxytocic he found it less prompt than quinine, but hastening labor and preventing hemorrhages when given for a week before confinement.

Kruse urged hydrastin for night-sweats, a full dose at bedtime. Others have confirmed this recommendation in phthisical and other forms of free sweating.

The eclectic applications of hydrastis as given in King's Dispensatory are numerous: The chief action is exerted upon the mucous and glandular structures, and through the hydrastine, upon the nervous system to some extent. It is valuable in disorders of digestion, functional, subacute and atonic with mucous flux; debility of mucosa; aphthous stomatitis, gastric irritability, icewater dyspepsia, gastric catarrh and ulcer, the best substitute for alcohol when stopping the use of the latter, with capsicum and strychnine; belching of putrescent gas, with sense of "goneness," preferably hydrastine in minute doses if there is great irritability; catarrhs of the intestine and gall-ducts, obstinate constipation, hepatic obstruction or congestion; convalescence from diarrhea or dysentery, in children; locally for fissured anus, hemorrhoids, ulcers and eczema of the anus, prolapsed and ulcerated rectum; catarrhal, follicular or granular pharyngitis; syphilitic ulcer of nose or pharynx, sore throat, rhinitis, ulcerated or aphthous tonsillar, pharyngeal or retropharyngeal catarrh; subacute nasopharyngeal catarrh where the mucosa are dry and parched, secretions altered in quantity and character; in catarrhal hypertrophy with profuse discharge and thickening of the membrane it has no equal; when mucus drops into the throat, ditto, used locally and internally; best if with catarrhs there is muscular debility; follicular and simple conjunctivitis, corneal ulcer, ciliary blepharitis, trachoma,

otitis media if free from granulations, eczema of the auditory meatus and irritation from wax, in all which it is used locally; myalgia, when worse on pressure or motion (Webster); often in reflexes from uterine, rectal and prostatic disease; reflex headaches involving the scalp muscles; pectoral tenderness from lacerated cervix; muscular pains due to hemorrhagic anemia; Schatz found it useful in hemorrhage from uterine myomas, congestive dysmenorrhea, hemorrhage in virgins even after curetting, hemorrhage from subinvolution, metritis, endometritis, parametritis, cicatrices, stenoses, and climacteric. He pronounced it too slow for post-partum hemorrhage, but good for passive forms and for metrorrhagia. Like ergot, it is useful for chronic cerebral engorgements, like congestions. It has been advised for fungoid endometritis, lacerated cervix and pelvic cellulitis; leucorrheas, vaginal and uterine; gonorrhea, gleet, with thuja; incipient stricture, spermatorrhea and cystitis even with ulceration (King); cervical erosions and light papillary vegetations; scrotal eczema, acne, seborrhea sicca or oleosa, scrofula, rosacea, lupus, sycosis, boils, carbuncles and ulcers (Jeanson) when dependent on gastric disturbance; it mitigates the severity of cancer, retarding its progress; in convalescence from maladies with excessive mucous fluxes or hemorrhages; or from general debility, protracted fevers, inflammations, and nervous prostration.

Specific Indications.—Non-acute catarrhs, and acute purulent otitis media, gastric irritability; irritation of parts with feeble circulation; muscular soreness worse on motion or pressure; passive pelvic hemorrhages; skin diseases depending on gastric disease.

Ellingwood says hydrastis resembles strychnine but its influence is more slowly developed and more lasting; it stimulates the respiration and circulation, imparting tone and power to the heart, and influencing blood stasis like ergot. Muscular tissue everywhere is thus influenced. It inhibits the development of superfluous muscular tissue. It increases the secretion of gastric and intestinal juices, and stimulates peristalsis. In cancer of the breast he gives hydrastis if the tumors are hard and painful, conium if small, hard and painless; phytolacca if soft or undulated, tender, with pain extending into the axilla. None of these is valuable if the cancer is open; all must be long continued and applied externally as well as internally.

The textbooks give the toxic actions of this drug and say scarcely anything of the effects of medicinal doses; so that one would draw from them the conclusion that it was unfit for remedial

administration. As a bitter tonic hydrastis has no superior, for all the uses to which such an agent may be applied. The uses of berberine are fully described in another chapter. The concentration should be dropped out of use, and whichever of the alkaloids is indicated substituted.

Hydrastine may be ranked with the strychnine group, and Ellingwood's differentiation adopted. The writer has repeatedly noted the slowness of hydrastine in getting to work and the singular endurance of its effects. Its property of giving tone to unstriped muscular fiber renders it useful in both constipation and diarrhea when due to relaxation. It is a dryer of mucous weeping. It checks hemorrhagic oozing. When the mucosa are worn out by long-continued over-stimulation, by alcohol or condiments, hydrastine will do more than any other remedy to restore functional activity. But in the treatment of hemorrhages it has been replaced by a better remedy, in hydrastinine.

The best effects of hydrastine are obtained from small doses long-continued. Give from gr. 1-67 to 1-6 before each meal and at bedtime, for a month before deciding on its value.

HYDRASTININE

Standard granule—gr. 1-12, Gm. .005.

Hydrastinine is an artificial alkaloid formed from hydrastine. It also forms in the plant under certain conditions, so that the galenic preparations of hydrastis usually contain some of this agent.

Hydrastinine causes little disturbance of the centers of motion and sensation, except in enormous doses (Santesson). The heart slows through stimulation of inhibition, an action analogous to that of aconitine. The arterial tension rises further than after hydrastine, and this effect lasts much longer. It does not depress the heart in medicinal doses. Cushny doubts the assertion that hydrastinine causes rhythmic contraction of the uterus and induces abortion. It acts solely on the uterine vessels, as on those of the rest of the body, and may cause death of a fetus by choking off its blood-supply.

Hydrastinine is soluble in alcohol, ether or chloroform, with difficulty in hot water, but its salts are readily soluble in water.

Falk concludes that hydrastinine paralyzes by its influence on the motor sphere of the spinal cord; it is not a cardiac poison; it effects vascular contraction partly by exciting the vasomotor centers but mainly by a direct influence on the blood-vessels. The rise

in vascular pressure is great and persistent. The pulse slows, before death the pressure falls and death from lethal doses is due to paralysis of the center of respiration.

As compared with hydrastine, hydrastinine does not cause spinal irritation or tetanus; has no injurious local effect; is not a cardiac poison, but an excitant, and death can be prevented by artificial respiration; the blood-pressure is much greater, has no interruptions of relaxation, and is the result of a steady contraction of the blood-vessels and not due to centric irritation.

Bunge found that large doses reverse the effects of small ones, by paralyzing the vagus. Hydrastinine does not destroy the red blood cells in any doses, large or small.

The most conspicuous effect of hydrastinine is a marked and persistent rise of blood pressure after moderate doses. The renal vessels are dilated (Paldrock). This is not followed by a compensating fall. Cotarnine acts as a hemostatic by lowering the vascular pressure through vasomotor depression.

Dr. Torgny Anderson, of Nebraska, reports: "During the last two years I have used hydrastinine hydrochloride to check bleeding—not the sudden and copious hemorrhages, for which atropine is best, but in the oozing, long-continued cases of bleeding. So uniformly satisfactory have the results been that I have come to look upon this drug as a sheet-anchor whenever and wherever continuous bleeding has to be stopped. The following three cases will show how varied its application can be and also with what good results it has been given.

Case 1. Mrs. S., American, age 36, married and mother of two children, large, strong and perfectly healthy with the exception of very profuse and prolonged bleeding during and after the menstrual periods, which condition began three years ago. Not only was the amount of blood increased, but while her menstrual periods had heretofore lasted four days, now it would be fourteen to twenty-one days each time. On the advice of a physician, at the beginning of the trouble, a surgeon had been called in and had advised an operation, probably curetment. She had been so sick from the ether administered that she told me she would rather die than go through another forty-eight hours like that time.

"After the operation menses were absent for three months, when the previous condition returned. I was then called in, and during the examination I scraped off with a blunt curet quite a lot of black, spongy mucous membrane from the uterine cavity. I could easily make out that the same condition existed all over the

uterine cavity. I advised a second curetment, but her experience with ether made her refuse.

"I had then used a hyoscine-morphine combination in several cases, so I explained to her its action and could confidently promise her that she would not be sick after the ether as before, and finally gained her consent. The curetment was done in the evening and I removed an ordinary teacupful of spongy black mucous membrane. One hour after the operation I awoke her and she told me that she had felt no pain. I then left for home.

The next morning, on inquiring over the telephone how she was, I was told that when she awoke after an all night's sleep she got up and began to dress. When her husband asked her what she was thinking of to get up the next morning after an operation, she answered that she felt so perfectly well that she had forgotten the operation, and very reluctantly went back to bed.

"Menstruation returned in six weeks and was normal for a half year, when the old trouble returned. I then gave her the hydrastinine hydrochloride tablets, one to be taken every three hours while awake until bleeding ceased. This it gradually did in seven days. I told her to begin taking them the same way from the first day of each succeeding menstruation. Between the menstrual periods I introduced wool tampons saturated in a vaginal antiseptic dissolved in glycerin. This was done every third day. Under this treatment the patient soon became normal in her menstruation. She has remained so now for nine months.

"Case 2. Mrs. K., Swedish, age 32, married. With the exception of more or less trouble with constipation she had always been well until about a week ago, when she began vomiting blood. A physician was called, and when after three days the hemorrhage still continued, consultation was decided on and a local surgeon and myself were called in. A diagnosis of ulcer of the stomach was agreed to by all three doctors. The surgeon advised immediate operation, and this was also the advice of the other physician, but I proposed the use of hydrastinine hydrochloride. The patient and also her husband would not think of an operation until every other way had been tried. So I began the administration of hydrastinine. The surgeon predicted failure—yes, even a fatal result—but in eight hours the hemorrhage had ceased and has not returned during the two years elapsed since then.

"Case 3. Mrs. McG., German, married, mother of nine children, 48 years old, large and fleshy. Menstruation had been very irregular for two years and had been entirely absent for one

year. A week before I was called in she had begun to bleed through the nose. A physician had been called and had partially succeeded in checking the bleeding but only as long as a clot remained in the nostril. As the clot hung down in the pharynx it caused vomiting spells, and when the clot loosened and was ejected bleeding began again. The physician used adrenalin chloride internally and liq. ferri tersulphatis locally on tampons.

"When I called I was told that for several months she had had a slight bleeding from the nostrils every month, corresponding in time with the time when she should have had her menses, but that she had not needed to call a physician until a week ago, when Dr. S. was called.

"I cleaned out the nostrils with an alkaline antiseptic and introduced tampons saturated with a strong solution of zinc sulphocarbolate. The tampons were not allowed to remain more than a few minutes each, when a fresh one was introduced. I also began the administration of hydrastinine hydrochloride, one tablet every two hours. For six hours hemorrhage ceased.

"The lady was so pleased with the result that she asked me to leave twenty tablets in case she should need them another time. As I have not heard from her since I take it for granted that she has remained well or that she is able to check the bleeding herself each recurring time by the use of the hydrastinine hydrochloride."

Therapeutics.—The action of this agent points to its use in any affection where it is desirable to limit the afflux of blood to the abdominal and especially the pelvic organs. Permanent benefits are therefore attained in congestive dysmenorrhea, virgins' menorrhagia with no evident lesion, and in retrouterine hematocele. In endometritis and in hemorrhages from disease of the adnexa it gives temporary relief. It palliates the hemorrhage from myomas for a long time. It does not cause contraction of the uterine muscular tissue and is useless in post partal hemorrhages. Nor will it excite labor pains or complete expulsion of the uterine contents at or before term. It is therefore not a substitute for ergot. But hydrastinine may possibly stop the hemorrhage of commencing abortion by astringing the bleeding vessels, and here it is safer than ergot.

Hydrastinine has been given with advantage for hemoptysis, and should be continued a week or two after the cessation of the hemorrhage (Hausmann).

Overdoses have been followed by uterine pains, gastric pain and nausea, pharyngitis, and rarely indurations or ecchymoses occur from its hypodermic administration.

As hydrastinine lessens the irritability of the motor areas of the brain, it has been suggested as a remedy for epilepsy (Cushny).

Keyser found hydrastinine, gr. 3 to an ounce of glycerin, useful as a local application for granular conjunctivitis. Shoemaker lists several forms of skin disease in which he uses it in lotion or ointment. Rousse pronounced it effective in uterine hemorrhages, phthisical night-sweats, hemoptysis, epilepsy and nephritis; hemostatic in congestive metrorrhagia, menorrhagia, hemorrhages after parturition and abortion, and from displacements or diseases of the adnexa, and those occurring during pregnancy and labor. It is useless as a hemostatic in myomas and cancer. Hydrastinine acts quicker than cotarnine, but is less enduring. Hydrastinine contracts the uterine and intestinal blood-vessels, cotarnine dilates them; the first is preferable for acute, the second for chronic maladies.

Hydrastinine increases intestinal peristalsis and the movement of bile. It may be employed as an agent to restrain mucous fluxes when not acute. Huchard advises hydrastinine for a week preceding menstruation in cases of metrorrhagia.

E. R. Fernandez reports three cases of uterine hemorrhage following miscarriage, in which hydrastinine acted satisfactorily as a hemostatic.

The dose of hydrastinine is from 1-2 to 1 1-2 grains a day, divided to suit the case. This is in serious hemorrhages; ordinary cases require about half these doses.

Reviewing the data available on the salts derived from hydrastis, it seems that all preparations of this plant might be abandoned except berberine and hydrastinine. The latter is superior to it in all cases for which hydrastine is used. The great cost of hydrastinine is the chief objection to its extensive employment; and unfortunately this seems likely to increase, as the plant is being extirpated and grows scarcer every year. English drug journals complain that the quality of the drug has deteriorated as it is no longer gathered by the Indians, and less care is taken to secure it at the season of greatest activity. The consequence is that the yield of alkaloids is small or wanting—a circumstance which, the journal quoted naively remarks, does not interest the preparer of galenic preparations. To the physician who has time and a tract of partially shaded land at his command, the cultivation of hydrastis offers inducements. The demand insures a market and the price makes it worth while, the crops realizing something like $1500 an acre at present prices.

HYOSCINE HYDROBROMIDE

Standard granule—gr. 1-1000, Gm. .0000625.

Hyoscine was discovered by Ladenburg in 1880. It exists in connection with atropine in varying proportions in every one of the mydriatic group of plants, but in none does it predominate, unless in exceptional specimens. For the rescue of this admirable remedy alkalometry is to be credited.

Hyoscine is a thick, syrupy liquid, but its salts crystallize. The hydrobromide is used by preference. It is readily soluble in water.

Physiologic Action.—Hyoscine resembles atropine in its effects upon the nerve terminals. The accounts of its action differ according to the purity of the article used. The pulse is slightly quickened, and the pupil dilated, some say more quickly than by atropine. Instead of stimulating the cerebrum, hyoscine causes a sense of fatigue and drowsiness in small doses, the patient moving and speaking less. In full doses sleep is produced, sometimes with a suddenness that is striking. The writer once administered a hypodermic of hyoscine gr. 1-100 to a patient, and then went out for four hours. On his return he found the patient standing exactly where he had left him, at the foot of his bed, sound asleep, simply having changed his posture by stooping. The sleep from hyoscine closely resembles normal slumber; the patient may be aroused if the dose is not toxic, and awakes refreshed.

The sleep lasts about eight hours. Sometimes slight confusion or even delirium precedes sleep. After full doses of the purest hyoscine, atropine symptoms are apt to follow.

Occasionally collapse has followed the use of hyoscine. The blood pressure falls, and respiration slows. Cushny says that tolerance is produced by its continued use, but the writer has given hyoscine in doses of gr. 1-100 for seven years, and the dose had only doubled in that time. This was in a case of paralysis agitans.

Sollmann says that hyoscine stimulates respiration, paralyzes the vagus and gland nerve-ends, and stimulates the heart muscle, like atropine. As a sedative and hypnotic in delirium tremens and in maniacal excitement hyoscine is preferable to morphine, since the former lessens the motor disturbance which morphine increases; and to chloral, as hyoscine does not depress the medulla so much. Hyoscine is remarkably well borne by the insane. Small doses have been found useful in paralysis agitans, lead poisoning and other tremors, and to allay spasm as in torticollis.

The physiologic action of pure hyoscine hydrobromide in the human subject may briefly be summarized as follows: Its mydriatic action is four or five times as pronounced as that of atropine; it is more promptly manifested, but is also more transitory. It does not exercise any appreciable effect upon intraocular tension, according to Rohlman of Dorpat, who claims that it is superior to atropine in eye-practice, and asserts that it can safely be employed in glaucomatous conditions in which atropine is inadmissible. When used too freely it is absorbed by the conjunctiva, and physiologic effects may be produced. Upon the central nervous system, instead of being an excitant and delirifacient like atropine, hyoscine is a sedative and hypnotic.

Therapeutics.—Hyoscine does not act equally well in all cases. Where it does, as a hypnotic, it leaves nothing to be desired; but in others, doses sufficient to affect the cerebrum are followed by annoying dryness of the throat and redness of the face and neck—in fact by atropine symptoms.

Cushny believes hyoscine to be less dangerous than atropine, as recovery has ensued when a dose of gr. 1-12 was taken, while 7 1-2 grains failed to kill a small cat. (It could not have been pure hyoscine.) But Shoemaker says that hyoscine is very much more powerful than hyoscyamine, and with this assertion we concur. The same author states that hyoscine may be used with advantage to allay the convulsions of cerebrospinal meningitis, to check spermatorrhea, and to quiet great nervous excitement with insomnia.

Hyoscine has been recently recommended as a hypnotic in the treatment of the morphine habit. The patient is duly prepared, the morphine stopped and hyoscine administered in doses of gr. 1-200, rising if well borne to 1-50, repeated as often as necessary to keep the patient in a stupefied state till the withdrawal period has passed. The doses are given every half-hour if necessary; in fact, whenever the patient shows signs of becoming conscious and troublesome. While several good observers have reported favorably on this method, it is repugnant to the principles that should govern the treatment of these cases, and we believe is a very dangerous method.

Dr. J. A. Rawls, of Iowa, used hyoscine as a hypnotic in a case of acute alcoholic mania, sleep following the sixth dose of gr. 1-1000.

The writer has found hyoscine valuable in anemic patients, and in insomnia without fever, adding aconitine for the latter; also in night terrors, somnanbulism, nocturnal convulsions, etc., when the causal indication has been met, hyoscine with cicutine hydrobromide has answered well.

Acute senile decay in an aged lady, with slow and irregular pulse and night terrors, screaming fits and suspension of assimilation and excretion—for this Fotheringham gave hyoscine gr. 1-100 by mouth in the evening, repeated in two hours when necessary, and in the morning, with an excellent recovery in two weeks. The same writer reported the success of this remedy in pneumonic meningitis with delirium, mild and severe hysteria, and delirium with rheumatic endocarditis.

Sexton reports extremely alarming symptoms from doses of gr. 1-100 which he seeks to avoid by combining morphine with it.

The therapeutic application of hyoscine to the relief of cerebral excitement was promptly made by clinicians, and in acute maniacal conditions and insomnia with agitation, hyoscine has largely taken the place of morphine. The ordinary dose for this purpose is stated to be one milligram (gr. 1-67); but much smaller doses (1-2 to 1-3 milligram, or gr. 1-125 to 1-200) given once daily, are in some cases followed by very marked muscular depression and hypnosis. It should therefore be given with due caution. Insomnia caused by cerebral excitement is rapidly quieted by these small doses, and a natural sleep follows. Certain cases of nervous asthma also experience great relief from hyoscine given in this way.

In the nervous erethism attending alcoholism, its sedative action is highly praised by Hare and others. Hyoscine hydrobromide has been used with advantage to allay the convulsions of cerebrospinal meningitis. It should also be of service in hiccough and in spasm of the laryngeal muscles. It has been utilized in cases of delayed labor to relieve excessive pain and irregular uterine contraction. In tic douloureux and histrionic spasm it may be injected locally, or one or two drops of a fresh one-percent solution dropped into the conjunctival sac. In cases of hysteria, the effects of fright or of strong emotion, this agent should be appreciated.

Magnan describes its effects as follows: "When we inject one-and-a-half milligrams of hyoscine hydrochloride into a patient who is a prey to a sharp maniacal excitement we do not at first notice any change in his behavior, but at the end of five or ten minutes, rarely more than that, the agitation becomes less, his movements lose their abruptness and rapidity—they last not so long. At intervals of some seconds the patient is quiet, holds still, and if standing up he does not gesticulate any more. His gait becomes shaky, uncertain and ill-coordinated. His muscular debility and incoordinate movements oblige him to lie down, and in fifteen to twenty minutes he can not raise himself. He tries yet to straighten him-

self up, but his legs do not support him and he lies down upon the floor. At the same time his loquacity becomes less, he is less voluble, and there are intervals of silence. The voice becomes more and more feeble, at times broken, trembling, and at the end of twenty-five minutes it is extinct; the patient does not speak any more, or utters a word now and then which cannot be clearly understood. General lassitude accompanies all these phenomena. When the patient sits up, his head droops on his chest, his eyelids close in spite of him, and he falls asleep. The sleep does not seem profound; he opens his eyes when you touch him, but falls asleep again. The sleep lasts five or six hours, and when he awakes he is quiet, sometimes for half an hour, but when the effect of the medicine has been dissipated, then the agitation and loquacity become again as bad as before the injection was made. There is habitual frequency of pulse, or tachycardia, dryness of the throat, thirst, and mydriasis persisting at times for three days."

Houdé says that: "Hyoscine is an antisecretory remedy, which gives good results in profuse perspiration, in alcoholic delirium and in phthisis. It is highly esteemed in asthma and whooping-cough, and as an antineuralgic; it gives excellent results in paralysis agitans, chorea, athetosis, sclerosis in patches and in writer's cramp. But it is most used as a sedative and hypnotic against psychomotor excitement. It is also prescribed for various kinds of insomnia.

We are assured by Messrs. Garnier and Cololian that we can by this remedy calm cases of extreme agitation (although it is only of value temporarily) and obtain also some hours of sleep. It is a powerful sedative, to which we may resort when we have to transport a furious patient to the asylum over a long road. It is a palliative but not a curative remedy.

It is usually administered by way of the subcutaneous cellular tissues, but it can also be given per os, or by rectal enema.

The usual dose is from one-half to two milligrams. Hyoscine acts on the inhibitory nerves of the heart in the same way as atropine.

When a dog had been previously curarized, and then has received hypodermically 7, or 8, or even 5 centigrams only of hyoscine, the heart will not be arrested when the peripheral ends of the pneumogastric are electrified with a very strong induced current.

A drop of a one-percent solution of hyoscine instilled into one eye of a rabbit or dog will produce, in seven or eight minutes, a marked dilation of the pupil, completely paralyzing the accommodation, then thirty minutes after that instillation the same effects are seen in the other eye, only less pronounced. On man the action is

even more pronounced; the paralysis of accommodation by the same strength may last for five days in the one eye, but the other one is not affected.

Hyoscine hydrobromide, says A. Robin, is not quite constant in its action as a sedative of the nervous system, for at times it acts in just the opposite way. He thinks that small doses judiciously administered, in cases of trembling, will give more regularity and satisfaction. In illustration he adduces a case of Parkinson's disease in a painter, who was so far cured that he could resume his labors and had only to guard against excitement not to bring on an attack. That patient was given from 1-10 milligram increasingly to 1-4 milligram of hyoscine *pro die* in the interval between December 4 and 24, 1901, when he was discharged.

Further experiments were made with this remedy in France by Drs. Lemoine, Malpilatre and Ramadier, on fifty-four maniacs who had each an injection of 3-10 milligram; thirty-eight enjoyed sleep for five to six and more hours. Usually there is no need to give higher doses, except that in cases which become accustomed, it may be necessary to advance to 1-2 or one milligram. In maniacs and alcoholics, Drs. Magnan and Loof give one milligram at the outset, which procures sleep for five to ten hours. The calming effect lasts for an hour or two after awakening, and then agitation and loquacity return.

The cases in which hyoscine can be employed advantageously are acute mania, alcoholic delirium and hallucinations, anxious melancholy, general paralysis with maniacal excitement, and in the periods of agitation before and after epileptic attacks. It can be utilized with great advantage in traumatisms of the insane, and generally whenever there exists the necessity to calm acute mania.

Magnan, who considers hyoscine as a kind of specific against agitation as a syndrome, admits that it makes the gait of the patient tottering, his movements to coordinate badly, his lower extremities numb, so that the patient rises with difficulty. One maniac said after hyoscine was administered to him: "My legs will not go, my feet stick to the floor." Another one said: "I have pitch in my pants which holds me fast to my chair."

Prof. Joly of Strasburg used hyoscine in twenty-three cases of mania, melancholy and dementia, with the following results: One-fourth of the cases got sleep at the end of seven hours; a seventh part at the end of four hours; and in a twentieth part the result was negative. In two cases in which the injection contained from .4 to .6 of a milligram the patient became pale, complained

of vertigo, heaviness of the head, and no sleep. The results were better when the remedy was given *per os* instead of hypodermically. But whatever be the mode of administration of the remedy the patient soon becomes accustomed to it and the dose has to be raised. It is best then to suspend hyoscine for a few days and use some other remedy for the while.

Hyoscine provokes disagreeable phenomena in nervous diseases without any cerebral affections. Brucher says it ought not to be used as a hypnotic until all other remedies fail, because it has a depressing effect on the entire body. Salgomendum of the Buda-Pesth asylum is of the same opinion, that its proper use is for calming alien agitations.

In ocular affections Drs. Trousseau and Remy have confirmed the rapidity and promptness of the medicament. From seven to ten minutes are enough to have the pupillary dilation come almost to an effacement of the iris. Atropine, duboisine and homatropine used in the same strength of one percent, and the same quantity, one to three drops, do not have such an intense and rapid action as hyoscine. The duration of the mydriasis is also longer, lasting for twenty-four hours just as strongly as immediately after instillation, paralysis of accommodation being complete. The strength of one percent is not painful and has no unpleasant reaction.

Trousseau and Remy have tried the remedy in fifty-two cases of all ages, and in various ocular affections, and found the results uniformly the same. It may be that hyoscine has a more important use in ophthalmic practice than it has hitherto been given credit for.

Rendle reports in the *British Medical Journal* the case of a young man, sixteen years of age, who suffered from chorea and was treated with bromide and chloride of arsenic without effect, and so too with morphine. The patient became debilitated, and the author got the idea of trying hypodermic injections of 3-10 milligram of hyoscine twice a day. After a little time a noticeable amelioration took place. The author then made the same injections three times daily. A week later the chorea had ceased, and the treatment was stopped. The convalescence was uneventful.

Dr. E. A. Robertson, of Montreal, says that a hypodermic of 3-5 of a milligram of hyoscine hydrobromide, administered before an anesthesia with ether, will prevent wholly or in greatest part the accidents which follow such anesthesia. The patient is soon asleep and remains calm so long as he is kept under the ether. The narcosis is rapid and requires but a small quantity of the ether. With this mode of procedure there is no hypersecretion of saliva or from

the bronchi, things which are so troublesome in the usual etherization. Nor is there vomiting, cyanosis or muscular rigidity. The patient may be easily aroused during the twelve hours of half-sleep following after such an etherization. Dr. Robertson never had to record the least alarming symptom that might be attributed to the drug. All the inconvenience it leaves at all is dryness of the mouth, and thirst.

It is well to remember in this connection that Dr. S. Marx of New York some years ago extolled the action of this drug in cases of accidents after cocainization of the spinal cord. (See *Semaine Médicale*, 1900, p. 406.)

Hyoscine hydrobromide may also prevent the vomiting after chloroforming, according to Dr. Stewart, as reported in the Australian *Medical Gazette*. The drug seems to be a specific against post-chloroform discomfort, provided the injection is made before the patient awakes. The dose required is half a milligram. Under these conditions there is nothing to fear. Dr. Stewart's observations seem to be conclusive.

From the above it will be seen that hyoscine is a medicament of high activity, which should be handled cautiously, small doses at the outset not exceeding a quarter of a milligram hypodermically. Houdé does not advise to use the syringe except when stomachal administration is impossible. Otherwise he advises one-fifth of a milligram, then gradually rising, if necessary, to two, three, four and even six milligrams.

A case of poisoning was reported in England, where by mistake a druggist gave about 1-14 grain of hyoscine at a dose. Deep coma ensued, as might be expected. The patient, a man of sixty-nine years, recovered within eleven hours.

Kraus describes a case of poisoning following the application of 1-120 grain of the hydrobromide of hyoscine to the eye. Four hours later the patient came to her parents' room, talking incoherently, with visual hallucinations, hands constantly grasping, speech very rapid. The room was in confusion, the patient nude. The symptoms lasted nearly four hours, when the patient fell asleep, and awoke quite well. The dose may have been exceeded, as patients are not always careful to limit the number of drops instilled into the eye.

Hyoscine is eminently a remedy for cumulative dosage. Some persons respond to doses of 1-1000 grain, and three such minute doses have caused disagreeable dryness of the throat, etc. Flaxen blondes, alcoholics and morphinists sometimes show exaggerated

sensibility to this alkaloid. Give gr. 1-1000 in solution, or directing the granule to be crushed in the mouth, and repeat every ten to thirty minutes until the desired effect has been secured. The dose thus established may be henceforth administered at once. Used with judgment hyoscine is one of the most effective sedatives and hypnotics at our command. It is safe, in that it is very rapidly eliminated, the third urinary discharge after its administration containing the last trace of it. Many "alarming cases" have been reported from its use, usually being the first applications of this alkaloid made by the reporter; but it is doubtful if death ever has resulted from hyoscine.

Prof. Wendell Reber, of Philadelphia, reports some exceedingly important investigations made by him in regard to the asserted identity of action of scopolamine and true hyoscine from hyoscyamus. These are especially valuable in view of the fact that the last edition of the U. S. Pharmacopeia authorizes pharmacists to dispense scopolamine when hyoscine is prescribed, and since the former is much the cheaper it is not likely that any other "hyoscine" will be dispensed.

In these trials one drop of 1-10 percent solutions of the two were applied, the hyoscine solution in the right eye, the scopolamine in the left, of the same patient. The utmost pains were taken to eliminate all sources of uncertainty. The alkaloids were both from Merck; the solutions were prepared by one of the most reliable chemists of Philadelphia.

In these experiments it was found that hyoscine required an average time of thirty-five minutes to produce full pupillary dilation, while scopolamine required an average time of forty-seven minutes to produce the same results. The average time for the onset of full cycloplegia under hyoscine was fifty-nine minutes, while scopolamine required ninety-two minutes. "So that the relative pharmacodynamic power of hyoscine hydrobromide and scopolamine hydrobromide, used in ordinary office work, may be said to be somewhere close to 59:92. Or, to reduce it to the commoner form of statement, hyoscine in these tests showed itself approximately 50 percent more potent than scopolamine in producing cycloplegia for refraction work.

"So much for the academic phase of the matter, which seems to be rather at variance with the claims that chemistry makes for these two drugs."

Correspondence is quoted with Merck & Co., in which it was first suggested that there might have been a difference in the specific

rotatory power of the two agents used, citing the fact to which we have frequently called attention, that there is much scopolamine of low optical rotation on the market; but in another letter Merck & Co. stated that the scopolamine and hyoscine furnished by them were both of the specific rotatory power of minus 20 degrees—and the hyoscine and scopolamine used in the test were both of Merck's manufacture.

The author goes on to say: "This leaves the matter precisely where it was in the beginning, namely, that with two drugs said to be absolutely identical as to clinical effect, pharmacodynamic power, molecular build and reaction with the polariscope, there should seem to be a more or less uniform difference in potency when tested by the delicate accommodation reaction."

There remains as a possible explanation the parallel fact of chemical identity, but pharmacodynamic difference, as also in the case of caffeine and theine, and of cocaine and stovaine, which are said to be chemical isomers and yet to exhibit a wide difference in their action. The familiar example of the kaleidoscope naturally occurs to one pondering such problems as these.

"It requires but a slight stretch of imagination to believe that some such similar principle may be operated among chemical isomers. That is to say, that although they may be of the same total molecular constitution, yet a different arrangement of the various molecules may result in difference of therapeutic effect or biologic reaction; just as one dozen dry or wet batteries produce currents of varying qualities according to the way in which they are connected, a fact utilized by electricians every day. Unless some such possible explanation as that just offered exists, there is no means of explaining the seeming difference in the reaction of the eye to hyoscine and scopolamine hydrobromides. In the last analysis it is always the clinical phase of such studies that interests us most."

In the discussion which followed, Dr. Albert E. Bulson, Jr., of Fort Wayne, Ind., agreed with Dr. Reber that hyoscine was more effective than scopolamine as a cycloplegic. For four or five years he had used hyoscine almost exclusively as a cycloplegic and found it more reliable than homatropine and more evanescent than atropine. He said it was absurd to think that toxic effects would not occasionally occur, notwithstanding the utmost caution. But in an experience of several thousand cases in which hyoscine was employed he had never seen any alarming symptoms, though frequently he noted toxic effects which warranted careful observation of the patient for some hours afterward.

Dr. S. D. Risley, of Philadelphia, was particularly interested in the peculiar isometric properties of duboisine, homatropine, atropine and hyoscyamine. While chemically identical, they produced very different physiologic results, especially in the duration of the paralysis of accommodation.

We have at last evidence from the source whence we have always claimed that the last word of the controversy must come—the clinical field—to show that hyoscine from hyoscyamus, and scopolamine from scopola are not identical in their action upon the human body.

Hyoscine and morphine were first proposed as an anesthetic for patients who could not stand the volatile anesthetics. Morphine gr. 1-8 to 1-4 with hyoscine gr. 1-100 were injected hypodermically, repeated in half or one hour if necessary, and again, when usually even a capital operation could be performed painlessly, or with the aid of the merest whiff of chloroform. Thousands have employed this combination with success. Some cases have been reported where alarming symptoms followed, but to those who are unfamiliar with the action of hyoscine its usual action may be "alarming," and too much weight is not to be given such reports. But in general hyoscine is preeminently a drug for the small dose rapidly repeated till effect.

The combination that has been established by the test of experience consists of morphine gr. 1-4, hyoscine gr. 1-100 and cactin gr. 1-67. The role of the latter has not been comprehended generally. It was first added as a heart tonic, to lessen any danger that might accrue from the depressing action of the other two ingredients. Cactin proved a useful addition, and when omitted or an inferior grade employed, the combination was found less satisfactory. It is now known that cactin relaxes vascular tension very quickly, admitting a speedier action of the analgesants, and quiets the nervous tension that offers resistance to anesthesia. Under the name of the H-M-C Compound Anesthetic, more than ten millions of these tablets have been placed in the hands of the medical profession up to the time of writing. These have gone to the rank and file, and have been utilized by the profession generally, under such circumstances as presented in the exigencies of general practice. It is scarcely fair to compare the results with those obtained by skilled specialists in anesthesia, in modern institutions, provided with every means modern science possesses to obviate danger and render the administration safe. Under such conditions the Mayo anesthetist reports over 15,000 ether administrations

without a death. No such result is approachable to the general profession in every-day work. Nevertheless, the H-M-C is able to bear comparison. Every effort has been made to trace every report or rumor attributing death to this anesthetic. Just eight cases have been found where the H-M-C may have caused death, but in not one of these is the evidence against the tablets conclusive and undisputed. This does not include reports from the application of scopolamine or combinations other than the H-M-C, which have been brought in to make out a case against the method. A comparison of these may aid in deciding the question of the therapeutic identity of true hyoscine and scopolamine. Nor does this record include deaths not justly attributable to the anesthetic but rather to avoidable errors in its administration, such as swallowing the tongue; or where six tablets have been administered within two hours in a case of gallstone colic.

The present status of the surgical application of this combination is tersely stated in a paper entitled "A Further Contribution on Hypodermic Anesthesia," by Emory Lanphear, M. D., Ph. D., LL. D., of St. Louis, Mo., Professor of Surgery in the American Medical College and Consulting Gynecologist to the Ellen Osborne Hospital. From this the following data are taken:

Historical Note.—When, in 1900, Schneiderlin made known his experience with a mixture of scopolamine and morphine as an agent for producing surgical anesthesia, Dr. Emory Lanphear of St. Louis, was much impressed with the importance of his contribution to surgical literature and early secured solutions made according to his formula. After about 75 operations under this form of anesthesia, with a fair degree of success in most instances, he was about to abandon further experimentation on account of (*a*) the reports of a number of fatalities—more than 20 deaths in some 400 anesthesias, according to Wood—(*b*) the occurrence of three deaths in St. Louis (one under his own administration), and (*c*) a number of alarming experiences in his practice, when his attention was called to a statement that scopolamine and hyoscine were identical chemically and probably so therapeutically. If this was true, why were we having so much trouble with scopolamine when we know from long experience with hyoscine (in other lines of therapy) that the latter drug is perfectly safe when used in even much larger doses than we were giving of the scopolamine? Believing there was a difference in the two he began using a pure hyoscine hydrobromide instead of scopolamine with the morphine. From the outset the alarming symptoms were absent—save for

cardiac depression now and then. Why the difference if hyoscine and scopolamine were, as declared by many, the same thing? And why was the price of hyoscine twice that of scopolamine if there was no difference between the two?

Thorough investigation, by correspondence with manufacturing chemists and by careful analytical work, showed these facts:

1. There is a hyoscine, of minus 20 degrees rotation, made from hyoscyamus niger only, which is free from impurities and perfectly safe in doses of one milligram (gr. 1-67) every hour, three times.

2. There is a scopolamine made by certain reliable chemists which is, also, of about the same degree of levorotation, which is certainly the same as hyoscine chemically and possibly may be so therapeutically; but in ordering tablets of scopolamine and morphine the surgeon has no guaranty that he will be given what he desires, for

3. There is upon the market a scopolamine, made from scopola atropoides, scopola carniolica, scopola Japonica and possibly other plants, which is of low rotary power (often as low as minus two degrees) by reason of the presence of atroscine, apoatropine or other impurities, very dangerous in some instances and almost inert in others.

For these reasons Lanphear has insisted that only hyoscine hydrobromide (made from hyoscyamus niger) be employed in the manufacture of the anesthetic tablets, since it has been found uniformly to be safe and effective.

After these hyoscine-morphine tablets had been used in a few hundred operations it became evident that, in many cases, the mixture would be better if it contained a heart-stimulant. Various drugs were tried; strychnine was found to interfere with the anesthetic effect, digitalin gave practically no effect until the operation was over, atropine caused delirium and did no good, gelseminine proved unsatisfactory, sparteine was too slow and made too large a tablet, etc., etc.; finally cactin (a concentration from cactus grandiflora) was tried and found to be the most satisfactory. Therefore, the formula decided upon consisted of

Hyoscine hydrobromide .....gr. 1-100
Morphine hydrobromide .....gr. 1-4
Cactin .....gr. 1-67

This is the tablet now so widely used for the production of surgical anesthesia. One of half this strength is made for obstetrical work and for the control of pain.

Safety.—Lanphear has now used this tablet in somewhat more than 2000 major operations—and has reports from thousands of other users who have made more than 10,000,000 injections; thus far only eight deaths have been reported and in some of these the cause has not been definitely shown to be the tablets alone.

It is true that many of these millions of tablets have been employed for control of pain only; but many thousands of surgical operations and labors have been conducted under their influence. Even in so small a series as Lanphear's 2000 cases (in which the injections were for serious operatic work) there should have been several deaths and many cases with alarming symptoms if this combination were at all dangerous—when given properly.

That there have not been more fatalities is remarkable, for this is a most potent mixture and thousands of these injections have been made in the country by men not wholly familiar with proper technic and sometimes perhaps not as careful as all anesthetists ought to be. For when used in conjunction with chloroform there is always a tendency, at first, to give entirely too much chloroform, the anesthetist failing to recognize the almost total anesthesia present before the inhalations are begun; in most instances a few drops only being required to put the patient into complete surgical anesthesia.

Everything considered, there can now be no doubt that, when properly used, hyoscine-morphine-cactin followed by a small quantity of chloroform or ether (or used in conjunction with a local anesthetic) gives the safest anesthetic known at the present day. But to gain the maximum of ideal anesthesia with the minimum of danger the following rules must be adopted.

Contraindications.—*Age-Limit.*—Full doses must not be used in patient over eighty or under five years of age. From fifth to tenth year half-doses are sufficient.

Never in Throat-Work.—It should not be employed in any operation in which the throat is to be opened or in which much blood will escape into the pharynx. This cannot be too strongly emphasized.

Not for Eye-Surgery.—It does not act well, alone, for operations on the eye. It is, however, of great usefulness in ophthalmic surgery when followed by a local anesthetic. One injection an hour and a half before operation so tranquilizes the nervous system that there is absence of fear, dread, anxiety, tremulousness, etc.

Kidney-Lesions.—Far advanced nephritis is a positive contraindication, as is also diabetes mellitus.

Precautions.—After the first injection is made the patient must be left alone—if allowed to talk a condition of intoxication follows instead of sleep; and after the second injection absolute quietude is essential to perfect results.

When brought to operating-table the patient must be gently lifted to it, not encouraged to walk to or to crawl on to the table.

If no other general anesthetic is to be used there must be silence in the operating-room—otherwise restlessness and excitation will occur so that considerable chloroform may be required to induce unconsciousness.

Before operation is begun the hands and (when possible) the feet should be tied so that a sudden motion may not interfere with the work. A sharp command to "lie still" with the further assurance "you shall not be hurt" usually suffices to control all movements, but sometimes a few drops of chloroform may be needed from time to time, as when strong traction is to be made on the peritoneum or the sphincter ani is to be divulsed; but, great care must be taken not to give too much—just a dozen drops or so may be enough to carry the patient into profound anesthesia.

With very old people one tablet given an hour and a half before operation usually suffices; with a trifling amount of chloroform at the beginning of work.

Since solutions of hyoscine and morphine deteriorate by standing, only tablets should be employed. The hyoscine-morphine-cactin tablets do not undergo any change—hence are always available and reliable.

Stomach and bowels should be empty as for any other anesthesia, since one may sometimes meet a case which requires much chloroform. But preliminary starvation is to be avoided.

When chloroform or ether is given, in addition to the hypodermic injections, the anesthetist must not depend upon the ocular reflexes—they are not abolished.

Miscellaneous Observations.—Women are more profoundly affected by it than men—which is true of any anesthetic.

Some persons insist upon talking or muttering throughout the entire operation, often complaining that there is too much pain. There is no remembrance of suffering afterwards in most cases.

The patient can be aroused at any time by shaking or loud command, but remembers nothing after consciousness is reestablished.

Disadvantages.—*Not Suitable to Minor Surgery.*—This combination should not be used for complete anesthesia for minor

surgery as it takes too long to get maximum effect and requires too much time for the narcosis to wear off. It, however, is excellent as an adjuvant to local analgesia in thyroidectomy, herniotomy and like operations, one injection being given about an hour before operation, then using cocaine, or better still anesthaine (stovaine), novacocaine, hydrochloride of quinine and urea, or other local anesthetic which may be sterilized by boiling.

Not a Local Anesthetic.—It is not, itself, a local anesthetic. Injected anywhere it produces anesthesia over the entire body. It is used just as any other hypodermic injection.

Want of Relaxation.—Alone it sometimes does not give perfect muscular relaxation, but a few drops of chloroform given by inhalation will overcome this when desirable, as in delicate intraabdominal work.

In Conjunction with Ether.—It does not work nearly so well in conjunction with ether as with chloroform; a single dose, however, injected an hour before operation, insures excellent anesthesia with far less than the usual amount of ether and overcomes the flow of mucus from the throat and greatly diminishes the feeling of distress of the early period of etherization.

Not so Effective with Drunkards.—Men who drink much liquor do not *always* act kindly under this anesthetic—they become excited, sometimes, rather than somnolent; yet a little chloroform will put them to sleep—far less than required when no hypodermic injection has been used, and with much less struggling.

With Morphine Users.—Finally it will not cause any marked degree of anesthesia in patients accustomed to large doses of morphine; here hyoscine-effect is conspicuous; flushing of face, intoxication or delirium, bounding pulse, etc. If a quarter of morphine sulphate be given in addition to the anesthetic tablet, when this condition is known in advance, much less chlofororm will be required; but usually it is best to give only the regular two injections and follow with enough chloroform to produce unconsciousness. Ordinarily after perfect narcosis is obtained very little additional chloroform will be required even in these cases.

Paralysis of Bladder.—In rare cases there is a temporary paralysis of the contractors of the bladder, so that for three or four days a catheter has to be passed. This promptly yields to two milligrams (1-30) of strychnine sulphate thrice daily, as a rule. If a half centigram (gr. 1-12) of calomel be given every hour for ten hours the day after operation there is generally no trouble with the bladder after the effect of the mercury is manifested.

Postoperative Acidosis.—From many careful observations it is decided that this condition is not so likely to occur in greatly prolonged operations under this anesthetic as when ether or chloroform is used. Possibly this is due in great measure to the fact, that patients do not have to be starved prior to hypodermic anesthesia. In only one of my cases has it been noted: amputation of the thigh for diabetic gangrene—the patient dying on the eighth day from diabetic coma.

Anuria.—Several deaths from total suppression of urine have been reported; but the proportion is no greater than occurs in ether-statistics. Should suppression of urine occur, it may be overcome by hypodermic injection of sparteine sulphate, 2 decigrams (3 grains) every two or three hours, and hypodermoclysis—one liter of normal saline solution in breasts or buttocks every four hours.

Too Long Slumber.—When two doses only are given the patient usually awakens in an hour or two and asks when the operation is to be performed. Sometimes the slumber continues six or eight hours and friends may become uneasy; but demonstration of the fact that the subject can be partially awakened at any time by rough shaking with sharp command satisfies them and usually permits refreshing sleep until the first keen pains have ceased. When three doses are administered the deep slumber may continue twelve to twenty-four hours but is not alarming unless patient becomes blue when he should be aroused from time to time or made to lie on his side if very fat. If sleep is too deep or too long, a pint of hot coffee may be given by rectal injection.

Post-operative Delirium.—A few cases of delirium have occurred, in two or three instances amounting to a mild kind of mania. It subsides after free purgation, with or without a few enemas containing two grams (30 grains) each of chloral and potassium bromide in starch-water.

Advantages.—The advantages of this form of anesthesia are many. Chief among these may be mentioned:

Absence of Nausea.—After operation there is absence of nausea or vomiting—a most important thing, especially in abdominal surgery.

Abolition of Pain.—Post-operative pain is conspicuous by its absence. Patients often pass a most comfortable night instead of suffering intensely, and sometimes sleep much of the first twenty-four hours succeeding operation, awakening next morning with a demand for food.

Early Feeding.—This desire for food may usually be gratified (except of course in operations on the stomach and other special work where peristalsis is objectionable) as the secretions are not checked enough to interfere with digestion. This prevention of semi-starvation is of great import in many instances, particularly when the patient has become weakened before operation and when there has been unusual loss of blood.

Prevention of Shock.—When this form of anesthesia is used, shock is absent unless there is excessive hemorrhage or unless too much ether or chloroform is used. Much of what has been called "shock" in the past was excessive amounts of chloroform, and in less degree ether.

Freedom from Fear.—A most prominent advantage of this form of anesthesia is the absence of fear or dread of the operation-room. The patient is brought in unconscious, or so nearly so as to have no sensation of fear, and the knowledge that there will be an absence of "that suffocating feeling" overcomes the chief objection to operation on the part of many patients. Besides, the advantage to the surgeon of not having to hurry "because the patient is not taking the anesthetic well" can scarcely be overestimated.

No Anesthetist Essential.—A most decided advantage of this form of anesthesia (and especially that variation of two hyoscine-morphine-cactin tablets at proper time supplemented by a local anesthetic when needed) is that a surgeon may perform many operations without the assistance of another doctor. The importance of this in country practice can hardly be overestimated. Curettage of the uterus, repair of cervix, repair of perineum, forceps delivery, operation for strangulated hernia, for appendicitis, reduction of fractures, etc., may be done with this agent, plus a local anesthetic.

Economy.—To hospitals, and to many doctors, the cost of ether or even of chloroform is something of more than passing interest. The average ether anesthesia costs about $1.00 (in addition to fee paid to anesthetist); that for chloroform about 35 cents; that for hyoscine-morphine-cactin about three cents when no chloroform is used, or 15 cents when it is; when local anesthesia is used instead of chloroform or ether, in conjunction with two of the anesthetic tablets the cost rises to six or eight cents for cocaine or to 10 or 15 cents for some of the newer, better agents.

In hospitals where many operations are performed, the use of even one tablet an hour or so before the patient is taken to the operation-room will reduce the anesthetic-bill of the institutions one-half or more.

Lessening Labor.—To the nurses this form of anesthesia is a God-send. The relief is not only physical but mental: no anxiety about post-operative pain, vomiting, restlessness, fear and thirst of the patient—all this means much to the conscientious hospital-nurse; and the patient who has had both forms of anesthesia can never again be induced to submit to chloroform or ether.

No Interference with Peristalsis.—Strange to say even when three doses are given there is but little if any interference with bowel-movement. An enema in twenty-four hours usually suffices and may not be necessary for not infrequently there is natural evacuation within the first day unaided. If not, there being no nausea usually, a cathartic such as a half centigram (gr. 1-10) of calomel may be given every hour, or citrate of magnesia or other saline laxative may be ordered.

Long Anesthesia.—The analgesia continues for many hours. This is of distinct advantage in prolonged, tedious operations. To know that the patient is not being carried to the brink of the grave by too much chloroform or ether is an immeasurable comfort to the operator who has to use a long time in his work.

How to Use It.—*For Beginners.*—Those who have not employed this form of anesthesia should begin by injecting one tablet one hour before operation; then completing the anesthesia by hypodermic injection of cocaine (or, better, stovaine solution for aseptic cases, since this solution may be sterilized by boiling) for minor cases or quick operations like thyroidectomy, strangulated hernia, superficial tumors, and the like. For major work or that which requires more than twenty minutes' time, the trial should be made with one hyoscine-morphine-cactin tablet an hour before operation, with anesthaine for the skin and hydrochloride of quinine and urea (1 1-2 percent solution) for deep infiltration; or with just as little chloroform as possible at time of actual work. The anesthetist will be astonished at the small amount of chloroform required for an hour's cutting.

For Minor Cases.—To do the best work with least discomfort to patient and least trouble to the doctor the following plan is best in minor surgery: An hour before operation one tablet is to be given, hypodermically, in the arm ordinarily, or in the neck, if the patient is very fat; then just before operation injection of some local anesthetic at site of work.

Under this form of combined anesthesia many operations can be done: amputation of fingers, opening of deep abscesses, dressing of lacerated wounds, removal of superficial tumors, and even those

of magnitude such as excision of tumors of the thyroid, buboes, castration, hydrocele and the like.

For Major Operations.—When time permits, and the severity of operation demands complete anesthesia, the proper method of administration is this: First injection of one full-strength tablet three hours before the actual work is to be begun, second injection an hour and a half later; at time of operation, if patient is not sufficiently analgesic to permit work, a little chloroform may be given by inhalation (or ether if preferred, though it does not act as well as chloroform) or an injection made with some local anesthetic agent.

Generally the patient is a little nervous or restless at the outset of the work but in a few minutes as soon as it is shown that there is to be no severe pain inflicted—this usually subsides. If not, a little chloroform may be dropped on the mask from time to time—*at the command of the operator, not at the discretion of the anesthetist,* for the surgeon better than anyone else can decide when the patient will need a little, as in cutting the skin, pulling on peritoneum, sewing up the wound, etc., while the anesthetist is invariably inclined to give too much. In tedious abdominal work (like resection of the stomach, enterostomy by suture, removal of the uterus) no chloroform will be needed, as a rule, except for opening and closing the belly; and very little for that in most cases.

When the patient is exceedingly robust and strong, and the operation is to be a prolonged one, three doses may be administered: One four hours, one two and a half hours and one one hour before operation. When thus given anesthesia will generally be perfect and effective for several hours; with slumber continuing from twelve to twenty-four hours.

After extensive experience, however, one finally reaches a point where the two-tablet method with the minimum amount of chloroform (or a local anesthetic) gives such satisfaction that no other form of anesthesia will be tolerated in the usual run of surgical work.

With Nitrous Oxide.—After the preliminary effects of the injection have become apparent the administration of a little nitrous oxide gas by inhalation gives ideal anesthesia. Experiments along this line have given most brilliant results in practice. This form of anesthesia is especially applicable to hospital work where facilities for the administration of the nitrous oxide are always at hand; but it is equally useful in operative work in private practice when the surgeon has the nitrous oxide in portable containers.

Dental Work.—For extensive dental work (operative, or sensitive filling or bridge-work) one tablet may be injected in the arm one hour before beginning; then from 0.5 Cc. to as much as 4 or 5 Cc. of anesthaine—according to the amount of pain to be inflicted—is to be injected into the gums. Mere application to the mucous membrane will not do. This amount of this stovaine mixture may be used without hesitation.

In Obstetrics.—Almost painless labor may be secured by this anesthetic agent, without danger to mother or child—*if properly administered!* If given in too large dosage or too near completion of the second stage there will be difficulty in some cases in starting respiration of the child; but when used rightly this cyanosis and difficulty with breathing will not be present.

In obstetrical work a full dose may be injected, in a primipara, whenever the "pains" become severely distressing. In one hour or more the patient's memory may be tested by showing a watch or other object and in ten minutes asking the woman what was shown her; if she does not remember, nothing more is yet needed, but if she readily recalls the object shown, one one-hundredth of a grain of hyoscine hydrobromide alone should be injected. In another hour or two if much complaint is made the memory-test is to be repeated and if indicated the hyoscine injection again given.

In most parturitions these three injections will give a labor which will be practically free from suffering. While the woman will cry out during the pains and often make much fuss from time to time there will be no memory of it next day.

With multiparæ it is better to give a half-strength tablet early in labor, then the hyoscine alone in an hour or two, and then another half-strength anesthetic tablet if progress be slow or if forceps are to be applied. In an hour after the second dose the instruments may usually be used without the knowledge of the patient, or at least without recollection after all is over.

When given in the manner above described this combination does not seriously interfere with the progress of labor; nor does it predispose to post partum hemorrhage.

For Severe Pain.—Since it does not arrest peristalsis or check the secretions to any serious extent this tablet is much used for the relief of severe pain like gallstone colic, renal colic, inflammatory disturbances, etc. It is of special benefit in controlling the pain in cases of great disaster: railway wrecks, mine explosions, extensive burns, and the like. In future wars the common practice will

be to give an injection of one of these tablets to every man seriously injured on the firing-line. This will not only relieve the immediate agony but prepare the sufferer for whatever surgical work may be found necessary on removal to the emergency hospital in the rear. Every ambulance surgeon, every military and naval medical officer, every physician in the employ of any railroad or other corporation liable to cope with severe traumatism should be provided with tablets of this kind.

Even morphine and cocaine habitues have taken hyoscine as a hypnotic for long periods without increasing the dose above gr. 1-100.

HYOSCYAMINE

Standard granules—Amorphous, gr. 1-250, Gm. .00025; crystallized, gr. 1-1000, Gm. .0000625.

Hyoscyamine was produced by Ladenburg in a state of purity about 1880, though it had been recognized by Geiger and Hesse in 1833. According to Merck there is absolutely no difference between atropine and hyoscyamine as to effects physiologic and therapeutic. Cushny says that while the resemblance is very close there are differences. Hyoscyamine is less stimulating to the central nervous system, the garrulous delirium of atropine being replaced by the symptoms of cerebral depression, fatigue, drowsiness and eventually sleep. The slumber is more like normal sleep than that produced by morphine; the patient is easily aroused and less confused. It is by no means constant, and atropine effects may appear instead. After atropine, sleep rarely follows. In fact, after studying Cushny's description, one suspects that he has been experimenting with uncertain and mixed samples of these drugs containing hyoscine. While some say that hyoscyamine acts more strongly than atropine on the heart, pupils and sweat glands, others deny this.

Huesemann and Hilger say that the two differ in that hyoscyamine causes a transient dilatation of the abdominal vessels, an elevation of the abdominal temperature and a diminution of that of the rectum.

Van Renterghem divided three milligrams of Merck's white crystallized hyoscyamine into six doses, and beginning at 7 p. m., took five of these at half-hour intervals. Twenty minutes after the first dose he felt dryness of the throat; at 7:40 the pulse became faster; at 8 redness of face and neck; at 8:30 sense of cold, light shivering; tongue and whole mucosa of mouth and throat dry, difficulty of speech; at 9:00, the mucous dryness was embarrassing,

impossible to insalivate any food, deglutition almost impossible, able to swallow with the aid of a little water, speech difficult, disposition to sleep, vision troubled, gait uncertain.

Excellent sleep followed, the experimenter rising twice to drink. Next day the throat was still somewhat dry, but all other phenomena had disappeared.

Therapeutics.—The consensus of experience seems to be that while hyoscyamine closely resembles atropine, the former is milder in action, less apt to cause delirium or to increase the pulse-rate, and disposes to sleep as an ulterior effect. It has been recommended in paralysis agitans, senile and mercurial tremors, neuralgia, acute mania, chorea, delirium tremens and epilepsy; in small doses it is narcotic and calmative; for vesical tenesmus, the delusions of persecution, spasmodic cough, laryngismus stridulus, hiccough, and whooping-cough. In all these hyoscyamine should be administered in very small doses, repeated every five to sixty minutes, till the first indication of its action is manifested in dryness of the mouth or throat, and then immediately suspended, as there will be no benefit derived from pushing the remedy beyond this point. It is best given in hot solution to secure the quickest effect, or in granules crushed and dissolved in the mouth. The dose of the amorphous alkaloid for such cumulative dosage is gr. 1-1000; and many persons will be found who cannot take the granule gr. 1-250 without unpleasant effects.

As a general rule we may consider the crystalline four times the strength of the amorphous; and to simplify practice, the use of the former is recommended.

In alienist practice hyoscyamine has been found useful in aggressive mania, chronic forms with hallucinations, subacute and recurrent mania, the irritative stages of general paralysis, and in epilepsy. Maniacs who tear their clothes quit this quickly and for a long time after some doses of hyoscyamine. Some have prescribed it with success in mania with periodic irritation, and in circular mania. Seguin preferred it to chloral in delirium. Sepilli and Riva found the access and gravity of epileptic seizures diminish under its influence. Kretsch advised against its use when hallucinations of vision were present. Lawson and Doerrenberg advised hyoscyamine for retention of urine and coprostasis of the insane, but Von Schroff preferred atropine here.

As an anodyne hyoscyamine has been employed largely. Oulmont injected it for neuralgias, tetanus, trembling paralysis, tremors of old age and of mercurialism, with complete success. Millican

gave it for hepatic colic, perityphlitis and asthma; Von Schroff as a calmative for coughs.

In America hyoscyamine has assumed an important role as a combined analgesic and antispasmodic. In the very numerous cases in which pain of a spasmodic form is to be conquered, this is the first of remedies. In the atrocious pangs of gallstones and urinary calculi, in all forms of colic, hyoscyamine has wholly replaced the less efficient and more dangerous morphine. Here full doses are needed, and glonoin is added to open the blood-vessels and secure prompt effect, with strychnine arsenate to steady the affected nerves, and this triad forms probably the most generally applicable anodyne-antispasmodic in our possession.

Abbott has placed hyoscyamine before the profession as a remedy for various forms of intestinal obstruction, such as impaction of feces, and strangulated hernia. Before resorting to prolonged and painful efforts at reduction, give a full dose of this agent, enough to produce redness of the skin, and often in a few hours it will be found that spontaneous reduction has followed the relaxation of the spasm that held the bowel imprisoned. The treatment of impaction, and of all but the suppurative forms of appendicitis, of perityphlitis, etc., by hyoscyamine has been advocated by Dr. Zophar C. Case, who has published a series of cases that would convince anyone but a bigoted adherent of the "no treatment but the knife" creed. The truth seems to be unknown to these gentlemen that in many cases the obstruction is spasmodic, and hence amenable to this potent remedy. These uses of hyoscyamine have rendered it one of the most important agents in our armamentarium. Between it and atropine the choice is generally a matter for individual preference. Possibly the anodyne effect of the latter is less pronounced.

Lanphear says prostatorrhea with an irritability of the deep urethra may be greatly benefited by the internal use of hyoscyamine; 1-250 grain may be ordered four times a day, alone or with 1-6 grain of concentrated hydrastin. If there is scanty urination much water must be drank and barosmin taken in doses of one milligram.

E. Maguire reports a severe case of renal colic, relieved completely and almost immediately by a milligram of amorphous hyoscyamine, dissolved in hot water and injected into the bladder.

In nervous insomnia, Trenel advises in addition to symptomatic remedies such as hot baths, the lactovegetable diet and the use of laxatives when needed, with careful attention to the excre-

tions, the methodic employment of hyoscyamine. This will even allow us to dispense with the baths. For tremors in general, paralysis, exophthalmic goiter, senile trembling, and paralysis of the insane, he found the same remedy applicable. This he attributes to its action on the great sympathetic. Convulsive neuroses and congestive affections of the cord and the brain, were markedly sedated by it. In all affections which depend on a congestive state of the nervous centers the physician will find this remedy, if not perfectly curative, yet far more than merely palliative. In paralysis agitans hyoscyamine calms decidedly the pains of the neck, diminishes the salivation, markedly reduces the tremors and affords sleep.

Cushny and Peebles conclude that hyoscyamine excels atropine in acting on the salivary glands and the vagus, also in dilating the pupil. Hyoscyamus illustrates the law that therapeutic experiments must be completed by human subjects, for pigs, sheep and rabbits find in this plant a harmless comestible; while to dogs and man it is toxic.

Hyoscyamine is eliminated unchanged by the kidneys and may be recovered from the urine. Ruatta found that a hypodermic injection of Gram 0.0015 induced light somnolence, dryness of the throat, dilatation of the pupil, and slight augmentation of the force and volume of the pulse, soon followed by a sensible diminution. Burggraeve pronounced it an excellent hypnotic and calmant, quelling the nervous erethism induced by large doses of caffeine or of coffee. It also facilitated diuresis, and is a good auxiliary to digitalis.

Laura uses hyoscyamine for nearly all forms of nervous and circulatory erethism, insanity, cerebralgia, the strong pains of meningitis, especially at the debut, all spasmodic affections, especially of the unstriped muscular fiber of organic life, bronchiolaryngeal spasm, intestinal spasm, that of the bladder, the uterus, the canals from secretory organs, the diverse forms of colics, even nephritic or hepatic, calculous or not, for asthma, angina pectoris, insomnia, nervous disquiet, in neuralgias even the obstinate sciaticas and in nervous palpitations. Peeters pronounced it an excellent medicament in acute mania, alcoholism and delirium tremens. It puts an end to troublesome priapism. Laura advises its use in the ordinary essential spasmodic neuropathies, whenever their seat is in the striated muscular fiber; as in chorea, eclampsia, and even in the habitual irritability of masturbators, and of epileptics. It relieves the insomnia that depends upon the special nervous states of various psychopathies.

To the genius of Burggraeve we owe the association of hyoscyamine and strychnine in the treatment of a great number of maladies, spasmodic and paretic, of the hollow viscera. This functional pathologic antagonism evident in the anatomic antagonism of the muscular or neuromuscular apparatus, he showed could be treated by the simultaneous employment of antagonistic physiotherapeutic modifiers (Laura). He says: "Hyoscyamine is the best of sedatives because it does not irritate. Conjointly with aconitine it calms the brain in insomnia. But it is especially in spasm that it displays its value. It comes to the aid of the surgeon in hernias momentarily irreducible, it stops contractions of the viscera, and it may be associated with strychnine when there is at the same time spasm and paralysis. With strychnine it forms an excellent remedy for seasickness, gastralgias, cystalgias, in a word, for all maladies of the hollow organs." Laura has used it in a great number of forms of mental alienation characterized by excitation, agitation and fury. Hoad employed it as a hypnotic in dementia with furious maniacal paroxysms, hysteroepileptic delirium, delirium tremens and in religious melancholia. Oulmont deduced these conclusions: Hyoscyamine presents all the active properties of hyoscyamus. The fixity of its composition gives to its action a precision never obtained from hyoscyamus. It should be given in small doses. He continued its use until slight symptoms of intoxication appeared, but this is rarely requisite. Laura utilized hyoscyamine in spasmodic and convulsive neuroses in general, in nervous tremors, senile and those of paralysis agitans, even obtaining from it some solace in tetanus. Oulmont utilized it in chorea, decided relief ensuing by the tenth day; Pitris in obstinate vomiting of pregnancy, threatening abortion; Joffroy in paralyses.

Empis gives a warning against the use of too large doses. Laura says it seems prudent to avoid it when the kidneys are seriously affected since hyoscyamine is eliminated by that route; but Damaschino, Bucquoy and Ferrand pronounce it inoffensive.

It is impossible to state beforehand the dose that may be required. It must be determined by the result of the administration. Of the very pure hyoscyamine employed in America, 1-500 grain of the amorphous or 1-1000 grain of the crystallized may be given every ten to thirty minutes in acute cases, or until beginning toxic action is denoted by dryness of the mouth or throat. Beyond this point it is unnecessary to go, in ordinary cases. The dose thus established may be given at once in chronic maladies, and repeated only after the evident effects have subsided.

Children take larger doses of hyoscyamine than adults, proportionally. Van Renterghem gives newborn infants one-eighth of a milligram at a dose, or about gr. 1-500. This seems a huge dose, and we suspect that this author has a weaker hyoscyamine than that used in American practice. Certainly his doses for adults, gr. 1-134 every quarter-hour, cannot be employed here. But Prideaux gave six milligrams—gr. 1-11—in acute mania; and Lawson 8 milligrams—gr. 1-8—in general paralysis of the insane. Seguin gave 50 milligrams at a dose in chronic mania—equal to gr. 5-6. The purity of the drug employed may well be questioned.

Poisoning with hyoscyamine is to be treated exactly as that from atropine.

Many other applications of hyoscyamine have been reported by American advocates of alkalometry. Thus Fretz met a case of delirium with retention of urine in typhoid fever. The patient would have required an anesthetic to permit catheterization. Hyoscyamine was given every fifteen minutes, and five doses gave relief. W. L. Day reported a case of gastric cramps where morphine had failed to give relief. Three doses of hyoscyamine and strychnine arsenate removed the difficulty.

George Mott gave hyoscyamine with codeine for thoracic neuralgia with bronchitis, relieving the pains and causing curious hallucinations of sight and hearing. H. I. Terpening reported the case of an aged paralytic with attacks of dyspnea and tremor, quickly relieved and cured in three weeks by hyoscyamine.

IODOFORM

Standard granules—gr. 1-67, Gm. .001; gr. 1-6, Gm. .01.

Iodoform, CHI_3, may be prepared by heating sodium carbonate, alcohol, water and iodine together. It occurs in yellow, shiny scales, soluble in alcohol and in ether but almost insoluble in water. It contains 96.68 percent of iodine, combined with the carbon firmly enough to resist everything short of decomposition of the molecule, yet broken up by solar light. In the animal body iodoform is decomposed, and eliminated by the kidneys, skin and lungs, mostly in the form of iodine salts, some being undecomposed.

Taken internally or applied to open surfaces, too long or in too large doses, symptoms of intoxication appear. These begin with a sudden acceleration of the pulse and slowing of respiration; the temperature rises at first, then sinks later; nausea, vomiting, anorexia and diarrhea follow. These disappear if the remedy is

suspended. If not, grave disturbances occur, excitement, insomnia, coma, hallucinations of persecution, mania, convulsions, and on recovery the memory may be weak. There may be continual anorexia with albuminuria and tube casts. A harmless exanthem and purpura may appear. The symptoms may persist for weeks, and end in death from heart paralysis, or a grave meningocephalitis.

Advanced age predisposes to iodoform intoxication, and the remedy must be employed with great caution in such persons, if at all.

Iodoform does not destroy the vitality of the tubercle bacillus, nor does it influence bacteria in general. The theory by which its beneficial action is explained is that it strengthens the affected cells in resisting the parasitic invasion—a theory unsatisfactory to those who have noted most closely the effects of iodoform in tuberculosis. No known decomposition product of iodoform exerts as beneficial an action.

Therapeutics.—Externally iodoform is used as a healing, anodyne and antiseptic dressing. For chancroids it has probably no equal. Old ulcers often refuse to heal because the sensory nerve terminals are exposed; when prompt and decided benefit results from the application of iodoform ointment. Irritable ulcers, such as frequently appear in the mouth, are quickly relieved and heal promptly when iodoform is applied—best in scales, not powdered. The pains of ulcerated cancers are relieved by it.

Internally iodoform has been employed extensively in the treatment of pulmonary tuberculosis. It soothes the cough and causes improvement in the affected region, but just how is unknown. It was first supposed to combat the bacilli directly; then that it disinfected the pulmonary tract, or interfered with the development of some of the bacteria concerned in the work of destruction; but, as with the *modus operandi* of internal antiseptics in general, the more they are studied the more difficult the problem becomes. The truth is, our knowledge of physiologic function is too imperfect to base upon it much of value as to the true action of remedies. Too often we must content ourselves with the knowledge that certain beneficial effects follow the use of a remedy, without being able to explain how the results are produced.

But when given to patients with pulmonary consumption, of any grade, iodoform brings about a general improvement, the cough moderating, the sputa healthier, and the disease processes apparently ameliorated. J. Solis-Cohen said that from iodoform he had obtained more benefit than from any other in treating this

malady. Chauvin and Jorissenne praised it as a remedy for hemoptysis.

Iodoform has been recommended as a remedy for neuralgia, catarrhal jaundice, the early stages of hepatic cirrhosis, syphilis, to check gastric fermentation, for dysentery, diabetes, tenia and ascarides. In fact, iodoform has been urged as a useful form for the introduction of iodine into the system; but except in tuberculosis this can better be accomplished by the use of iodized calcium or the iodides of mercury, iron, arsenic, etc.

Shoemaker suggests the following test for approaching iodoform intoxication: Mix a few drops of urine with calomel, stirring with a glass rod, on a white plate; if iodine is being eliminated in dangerous quantities there is produced a well-marked yellow discoloration.

No application appears to have been made as yet of the power of iodoform to increase the thyroid secretion. The same is true of Binz' discovery that iodoform hinders the diapedesis of leucocytes.

Iodoform has been advocated as an intestinal disinfectant, but there are other and more reliable agents, less dangerous.

F. Warren Lanoix found that the headache affecting miners from the fumes of blasting powder was quickly relieved by inhaling iodoform from a bit of gauze.

Sollmann attributes the antiseptic action of iodoform to a slow liberation of iodine. Granulation is also thereby stimulated, and infection lessened or prevented. Sodium bicarbonate has been proposed as an antidote. Iodoform is slowly absorbed from the intestine, which indicates the propriety of small and frequent doses, as the danger of accumulation is thereby avoided. Irritation of the eyelids or of the nasal mucosa should be taken as an evidence of beginning toxic action, when the remedy should at once be suspended. Moleschott employed it to induce absorption of serous effusions, and for mitral insufficiency without compensatory hypertrophy; but Laura prefers as more effective, digitalin, strychnine, caffeine and convallamarin. He has obtained from iodoform rapid and manifest benefits in mild and chronic engorgements of the glands and the articulations. Others have utilized this remedy for uterine and ovarian engorgements, and for chronic uterine catarrhs. Laura praises it in mild and chronic bronchites, finding it a good soothing expectorant, even in grave and advanced tuberculosis. In bronchopneumonia and especially in caseous bronchoalveolitis Semmola and Chiaramelli employed it; while Kuffner also testified to its value in treating tuberculous laryngitis. Moleschott, Coes-

feld and Bauer used it in tuberculous meningitis, and Spitzka announced a series of cures resulting from its application to the shaven scalp. Ciattaglia and Laurensi applied it to the cure of syphilitic neuralgias, Kennedy, Hamilton and Condie to periodic neuralgias and even to intermittent fevers. Ruatta found it useful in chronic metritis and engorgements of the prostate, as an anesthetic, resolvent, cicatrizant and disinfectant. Plevani applied a mixture of iodoform, quinine and charcoal to ulcerating uterine cancers, as a palliative. Laura finds it sedative, in small doses, in hyperesthesias, nervous erethism, spasmodic coughs and dry bronchitis. It regulates cardiac rhythm and gives more force to the systolic contractions, so that it is useful in all cases where the heart's force is lessened without compensation. Burggraeve pronounced iodoform a diffusible stimulant and a calmant or anesthetic. He prescribed it in irritative affections of the prima via. It does not suppress but incites the secretions, when vitiated as in the late stages of phthisis, in all lymphatic maladies, where it activates the sanguine crasis. Besnier gave it internally as a remedy for lupus erythematosus. Schildowsky attributed anthelmintic powers to it, especially against nematodes.

Those who are unaccustomed to the powers of small frequent doses should be careful with iodoform. Give a milligram every half hour, or a centigram every two hours, and not a grain at a time as under the old method—and better results will follow from much smaller quantities of the drug. As an anthelmintic full doses should be employed.

Iodoform should be given by the intensive method. The dose should not exceed gr. 1-6, and for very susceptible patients the granule of gr. 1-67 should be used. One of either may be given every hour or even oftener, till the patient begins to taste or smell the drug, which is an evidence of saturation, when it should be discontinued or given in smaller doses or less frequently. Tuberculous patients evince a remarkable tolerance for iodoform, and the writer has given fifteen grains a day to these patients; but it is better to use europhen, which is less apt to cause toxemia. Some persons evince an idiosyncrasy against all these iodic compounds, and this may even be hereditary. The writer once applied a very small dusting of europhen to an anal fissure and next day an intertrigo had developed that took off the epithelium from the umbilicus to the knees. The daughter of this patient was similarly affected by the same agent; and both proved refractory to all forms of iodine, locally applied.

IRIDIN

Standard granules—gr. 1-67, Gm. .001; gr. 1-12, Gm. .005.

Iridin is a resin derived from the Iris versicolor, or blue flag.

Felter and Lloyd attribute the virtues of iris to the oil, which is a constituent of iridin.

The same authors say that iris acts upon the gastrointestinal canal, the glandular and nervous systems; powerfully exciting the biliary, salivary and pancreatic secretions. It causes violent acid vomiting, frequent hydragog catharsis, intestinal burning and severe colic. After fatal doses, marked gastrointestinal congestion is found. It has produced neuralgia of the face, head and extremities. It causes salivation but without injuring the gums or the teeth. It is alterative and cholagog, one of the best agents to influence waste and repair, exerting a powerful catalytic action upon the lymph glands, the ductless glands, the liver, pancreas and kidneys. It does excellent service in cachexias, bad blood, scrofula and mercurialism; and in secondary syphilis with cerebral disturbance and coppery skin it is one of the best remedies. For biliousness it is prompt and efficient; for bilious headache with nausea and bitter vomiting or sick headache from indigestion it is unsurpassed. Other conditions for which Felter and Lloyd recommend this agent are: Chronic hepatitis and other hepatic affections with constipation and sharp, cutting pains increased on motion; duodenal catarrh with jaundice and clayey stools; constipation from torpor; in minute doses for gastric irritation in cholera infantum and morbus; diarrhea and dysentery with large, slimy evacuations; gastralgia; aphthæ, reflex muscular pains from gastrointestinal or pancreatic disorders, especially when the muscular coats of the viscera are affected; pectoral and subscapular pains; soft, glandular enlargements; goiter or enlarged thyroid—one of the few reliable drugs here—whether constant or menstrual; ovarian and uterine disturbances with goiter (use internally and locally); exophthalmic goiter in early stages; it improves Addison's disease; chronic pancreatic diseases with sodden, lead-colored tongue, chronic splenic disease with white skin—leucocythemia; chronic renal diseases, ascites, anasarca, hydrothorax, hydroperciardium (in dropsies given in cathartic doses, with ginger, piperine or camphor); uterine hypertrophy, enlarged ovaries, ulcerated os and cervix uteri, uterine leucorrhea and dysmenorrhea, especially with impaired health, mental depression and pigmented skin; chronic and syphilitic rheumatism,

gonorrhea, spermatorrhea and prostatorrhea and nocturnal emissions from masturbation, with debility, mental uneasiness and centric nervous irritation; syphilitic iritis (Scudder); malarial jaundice, intermittent and bilious remittent fevers, with euonymin; for vomiting of pregnancy give iridin 3 gr. at bedtime with a saline in morning; comedones and other skin affections of youth, chronic, with genital disorders, rough greasy skins; full thyroids in women; syphilides, eczema rubrum of children and capitis of adults, zoster and herpes preputialis, given with rhus; rupia and impetigo with sulphur or arsenic, lepra; pustules on head in children; in all cases associating other indicated remedies.

Specific Indications.—Thyroid fulness, enlarged spleen, chronic hepatic disease, with sharp, cutting pain worse on motion; nausea and vomiting of sour liquids or regurgitation of food, after rich pastry or fats; watery, burning stools; enlarged lymphatics, soft and yielding; rough, greasy skin with sebaceous disease; menstrual wrongs with large thyroid; unilateral facial neuralgia; wasting muscles and other atrophies, and bad blood.

Ellingwood says that iris promotes waste and elimination of effete material from the blood. It will prove serviceable when the stools are clayey, urine scanty, skin inactive and jaundiced; in digestive irritations with altered secretions; neuralgia over right eye; acid nausea with gastralgia, after rich food; burning diarrhea; cholera morbus with violent umbilical pain, serous stools and great depression.

Henson claims that only the green root preparations are active, and that they rival phytolacca in their beneficial effect on diphtheria and tonsillitis. He pronounces the drug a mild hepatic stimulant, with an especial curative effect on the stomach resembling that of sodium sulphite. It acts on the pancreas, a power shared only by iodine, mercury, and perhaps mandrake and cinchona. The key to the use of iris is when the spleen and pancreas are affected as well as the liver, with sour stomach, vomiting acid or yeasty half-digested food an hour after meals. If the liver is also torpid add podophyllin; for constipation, aloes for men, juglandin for women; or cascara for either. If the whole alimentary canal needs toning, give hydrastine, which will relieve the diarrhea.

Laura finds iridin tonic and stimulant, useful as an antidyspeptic and purgative, with some cholagog property, that may be utilized in hepatic engorgements and in functional disorders consequent. It does not irritate the rectum. Its field lies in combating torpid gastric and intestinal indigestion. Mild intestinal catarrhs

of the bowels may be relieved by it, and its diuretic power renders it suitable for edemas and internal serous effusions.

Van Renterghem took Merck's iridin up to doses of a gram, without much effect. But this is one of the remedies that requires bile to develop its activity; and the small granules made with inspissated oxgall are active. Ellingwood gives the dose of the oleoresin as one to five grains. The eclectics employ specific iris in doses from a fraction of a drop up to five drops. They do not employ iris as a cathartic. For chronic cases it seems best to give small doses, gr. 1-67 to 1-6 before meals and at bedtime, increasing as may be indicated, and watching the stools for the effect, rather than begin with large irritative doses.

IRON

Standard granules—Iron arsenate gr. 1-67—1-6, Gm. .001—.01; iron iodide gr. 1-12, Gm. .005; iron phosphate gr. 1-67—1-6, Gm. .001—.01; iron valerate gr. 1-6, Gm. .01.

Cushny says that iron is probably essential to all forms of protoplasmic life. Small doses of the persalts of iron have an astringent taste; in larger doses they cause pain and nausea, vomiting and even purging. The gastrointestinal disorder may be so severe as to occasion collapse. The prolonged use of iron causes dyspepsia, constipation and colic, if the iron collects in the bowel in the form of sulphide. Blackening of the teeth may be caused by the acid present, by the formation of iron sulphide, or by the union of tannic acid from the food with the iron. Iron increases the secretion of hydrochloric acid (Budygan). The salts of iron with organic acids hinder digestion more than the salts with inorganic acids, ferric salts more than ferrous, and the insoluble salts the least of all. The digestion of starch is scarcely affected by iron. Given by the mouth iron induces leucocytosis (Pohl), and does not affect the renal excretion of double sulphates, hence has no intestinal antiseptic action (Moerner).

When the double salts of iron are injected into the blood they occasion toxic symptoms, disturbed respiration, gastrointestinal disturbances, casts and albumin in the urine, the post-mortem showing the gastrointestinal mucosa congested with extravasations. The kidneys are also congested. In acute poisoning the alkalinity of the blood is reduced by the lactic acid formed. The effect on the central nervous system is depressing, even to paralysis, but this may be due to the gastric effects. Very large doses dilate the blood-vessels. The astringency is due to the precipitation of proteids.

When iron is injected into the blood about 2 to 5 percent of it reappears in the urine, the rest being stored up in the liver and spleen, and possibly in the marrow, whence it is slowly taken by the various tissues, and excreted by the mucosa of the large bowel. Iron is absorbed by the duodenal mucosa, carried along the lymphatics to the blood, stored in the spleen, taken through the portal blood to the liver, stored there for a longer time, and slowly distributed through the blood, finding its way out through the large bowel. Nothing is known with certainty as to the form in which iron is absorbed. It passes through the thoracic duct to reach the blood. While there is usually plenty of iron in the food, there is decided benefit from the administration of iron as medicine. This is explained on the theory that the food iron is so enveloped in colloids that its absorption is hindered.

Sollmann, quoting Tartakowski, says that all iron compounds are converted in the intestines into loose organic compounds, and absorbed as such, mostly from the duodenum. Some may be eliminated with the feces. From the blood the iron is deposited as ferratin granules in the liver and red marrow, spleen and a little in the kidneys. Here it remains until utilized or excreted. This occurs mainly through the intestines, in the form of a firm organic compound. It is transformed into hemoglobin as needed. Excessive absorption simply increases this reserve stock. When this is exhausted recovery from disease only occurs if some form of iron is given. Iron acts in the stomach and bowel as an astringent, and in large doses it constipates. It does not irritate the kidneys. The brilliant success of iron in chlorosis indicates that in that disease an extraordinary quantity of iron is needed.

Therapeutics.—The presence of iron in the blood and every tissue sufficiently justifies its use as a nutrient tonic. When given in proper remedial doses iron increases the appetite, stimulates the digestion, tends to check diarrhea if present and to constipate if diarrhea does not exist. The blood improves in quality, the color freshens, the eyes brighten, and the pallor of anemia gives place to the rosy hue of health. When the smallest doses of iron are given, most of it appears in the blackened stools. Very little is absorbed, and this has led some authors to recommend doses too small to cause this blackening. But experience has shown that a certain percentage of the daily dose is absorbed; and that if the dose is increased to full tolerance, the same percentage of this larger dose will still be absorbed. Hence the rule promulgated by Niemeyer in cases of chlorosis, to give all the iron the stomach will

bear; and the results of this medication he pronounced the most brilliantly successful in the practice of medicine. But when iron is thus given there is a tendency for large quantities to accumulate in the bowel in the form of an insoluble sulphide, which may cause obstruction or ulceration. This accident may be prevented by administering a dose of some saline cathartic, sufficient to clear the bowels of the ferruginous accumulation, every two or three days.

It has been found that when nuclein solution is given at the same time as iron, the proportion of the latter that is retained in the body is increased.

Iron is useful in all cases of anemia, whether essential or due to organic disease, with exceptions to be hereinafter noted. It thus relieves many affections that depend upon anemia for their presence, such as amenorrhea, neuralgia and various neuroses, dyspepsia, etc. When there is a cause of the anemia evident it is of course to be treated as well, and neglect of this simple rule is the reason many persons improve while taking iron and drop back when it is discontinued. Thus, if the anemia be due to constipation and fecal absorption, it is folly to give iron without at the same time regulating the bowels.

Iron is thus given for anemic dropsy, in convalescence from fevers, the cachexias of malaria, syphilis, mercurialism and chronic diseases. In asthenic erysipelas the tincture of the chloride of iron has done the greatest good of any remedy the writer has ever employed, when given in full doses—a dram every four hours—but in the sthenic form it is worse than useless. The perchloride is the most effective of the local astringents.

Iron in small and frequent doses is efficient for passive hemorrhages, and when postpartum bleeding has been reduced to a dribble which yet resists ergotin. But diathetic bleeding is increased by iron, and in some cases postpartum hemorrhage will continue as long as iron is given. When hemorrhage continues from anemia, it is wise to give the salts of lime to restore strength to the blood-vessels and then the iron will accomplish its work far better.

In desquamative nephritis iron has been largely given, the use of Basham's mixture being a routine with many practicians. The writer has never known of benefit from it; though the anemia resulting from this malady may be benefited by iron provided elimination is perfectly unobstructed. Otherwise iron is apt to do harm.

As iron increases the excretion of urea and the frequency of micturition, it deserves to rank among the diuretics; but this power has only been utilized in treating the dropsies of anemia.

Smart says the sulphate is the best chalybeate to increase the number of the red blood corpuscles and their hemoglobin, the carbonate ranking next and the chloride third.

Shoemaker mentions as adapted to the use of iron, subacute and chronic eczema with anemia; pseudoleukemia, acute rheumatism in anemics, to alternate with mercury in debilitated syphilitics, chorea (iron bromide), gonorrhea, leucorrhea, tuberculosis, anemic hysteria with amenorrhea, for neurasthenia with palpitation of the heart, anemic puerperal mania and that of lactation; rachitis; profuse mucous discharges, dilatation of the stomach, thread worms, emphysema and phthisis; fatty and dilated heart; nocturnal incontinence of urine; spermatorrhea with relaxation and anemia; vasomotor disturbances of the menopause.

The contraindications for iron are: Plethora, the apoplectic tendency, hypertrophy of the heart; acute fever, of the sthenic type especially; active hemorrhage, and the hemorrhagic diathesis; florid phthisis, where the use of iron was shown by Trousseau to induce hemorrhages from the bronchi; active gastric catarrh, and acute affections of the stomach or intestines, which are made more active by iron.

When persons long anemic have their blood improved by iron, they are apt to suffer from headache, the brain having been accustomed to the thin blood. This may be prevented by giving iron bromide, or by adding a little hydrobromic acid. Usually all that is needed is to keep the bowels free and aseptic.

When the object is to improve the blood as quickly as possible, it is best to keep some iron constantly ready for the absorbents, by giving quite small doses very frequently. Of iron phosphate gr. 1-6 may be given every half-hour during the day, and this dose may be increased to a grain if well borne. Much more will be tolerated and absorbed in this way than by the old routine of three doses a day.

In the long list of chalybeates there is room for endless variations as to combinations with other salts, and individual tastes, conditions and idiosyncrasies. Numberless attempts have been made to establish the superiority of some one or other salt of iron, on the score of assimilability, etc., but investigation has invariably disproved these claims, and shown that all iron salts and preparations are useful in the treatment of anemia. Even iron filings and the scales scattered from the smith's anvil have proved beneficial. The best preparation is that which best agrees with the taste of the patient and disorders his digestion least, and hence can be given in the largest doses.

All the tonics are synergistic to iron, as well as the whole tonic regimen of cold or salt baths, high feeding, open air, mountain or sea-shore, exercise, etc.

IRON ARSENATE.

For the uses to which iron is put as a reconstituent tonic, the arsenate is undoubtedly the best of the chalybeates. While iron is an antidote for arsenic, acting by rendering the latter insoluble, this insolubility is not absolute but relative, and prompt evacuation of the stomach must follow the use of the antidote.

Burggraeve pronounced iron arsenate the reconstituent of the blood, *par excellence.* "The blood is a *milieu* from which all the tissues draw the elements for their reconstitution. In cancer, tubercle, scrofula, it prevents the development of morbific germs while favoring the transformation of white cells into red. Looking on pathologic elements as physiologic elements diverted from their true place, we may hope to return them by amending the nutritive processes. This is what iron arsenate does. In squamous skin diseases, lichens, psoriasis and lupus, it is necessary to modify by a powerful nutrition, a fertilized soil, the renovation of the epidermic cellules. Here it is still the blood which should be improved. And who can say that it is not the elementary white globules of this liquid that furnish the innumerable cellules constantly in the process of formation and transformation? There is always the formative nisus, vitality; but if the material does not possess the spontaneity of evolution, the life cannot abstract itself from the matter."

For anemia with weak heart and edema he associated iron arsenate with digitalin, to rapidly reestablish the normal respiratory and circulatory rhythm. He also employed this agent for chloro-anemias from delayed menstruation, the purulent cachexia, etc.

Hare recommends iron arsenate in anemics with dry, scaly skin diseases; and in the anemia of chronic diarrhea.

The dose is gr. 1-67 to 1-6 before each meal, or the smaller dose every half-hour while awake. It is well tolerated.

IRON IODIDE.

Iron iodide is remarkable from the fact that both the elements contained in it exert their effects at the same time, though these are to some extent antagonistic. It is especially suited to cases of scrofula, where there is need for stimulating the destruction and removal of morbid material and rebuilding healthier tissue at the same time. The iodine in this combination is very active, and care must be taken that overdosing does not occur. The first intimation

of irritation of the eyes or nose, coryza, sneezing, should be the signal for lessening the doses or suspending the remedy. It is best given to adults in doses of gr. 1-12 every two hours.

In anemic syphilitics this is useful and may be given with the iodides of mercury, arsenic and lime; also in non-pulmonary tuberculosis, and amenorrhea with lymphatic enlargements.

IRON PHOSPHATE.

Iron phosphate is well suited to any of the uses of iron for which the arsenate is undesirable. Whether the phosphoric acid combined is useful in any given case or not, it is at least harmless.

IRON VALERATE.

This preparation unites with the properties of iron those of an antispasmodic and nervine. It possesses the powers of valerian in sustaining the nerves and comforting the afflicted which render that remedy so valued.

JALAPIN

Standard granule—gr. 1-67, Gm. .001.

Jalapin is a resin from Ipomœa Jalapa. This resin contains two glucosides, convolvulin and jalapin, the latter in small quantity. It is a drastic hydragog purgative in large doses, requiring bile to develop its activity. Full doses produce stools in two hours, with much pain and griping. Toxic doses cause acute enteritis, with bloody stools, but a less degree of gastritis as evidenced by nausea and vomiting. But moderate doses are less apt to cause griping than the aloes group. Jalap is a local irritant to the skin and mucosa.

Jalapin increases intestinal peristalsis and is well suited to cases where hard scybala form. As a purgative to clear the bowel in the beginning treatment of fevers jalapin is suitable; also as a derivative in cerebral congestions and similar states of the spinal cord. As to dropsies it is now well comprehended that the weakening from hydragogs more than counterbalances the benefit derived from the excretion of fluid. There are better and safer ways of accomplishing this object.

Jalapin like all purgatives is contraindicated in acute intestinal irritations and inflammations, menstruation and pregnancy, collapse, asthenia and anemia; and in cystitis those drugs that act on the lower bowel should be avoided. Dissolved in glycerin from one to three drams, jalapin acts effectually when injected into the rectum.

Shoemaker recommends jalap in congestion of the lungs with distended right heart, lividity, short breath and cardiac asthma.

Felter and Lloyd recommend jalap in inflammations of the biliary apparatus; costiveness, hemorrhoids; taken before meals as a remedy for excessive appetite, and to hasten expulsion of worms.

Specific Indications.—Costiveness; pain and griping in lower bowel; colic with stercoraceous vomit; general gastrointestinal torpor.

As a cathartic jalapin is only employed in combination with other drugs of this class. Given in the small doses of gr. 1-67 every one to three hours it excites peristalsis and intestinal secretion and thus relieves costiveness and habitual constipation. But unless carefully dosed and the influence of habit is established, the doses must be increased and the effect is not curative. As a cathartic for prompt and free action the dose is two to five grains; best given with a full dose of potassium bitartrate. It then acts in two hours. Given in glycerin by enema the dose is one grain.

Van Renterghem recommends gr. 1-3 every hour for an adult.

Burggraeve advised gr. 3-67 hourly in chronic enteritis.

JUGLANDIN

Standard granules—gr. 1-67, Gm. .001; gr. 1-6, Gm. .01.

Juglandin is a resin from the root bark of Juglans cinerea, the common butternut. That employed by French dosimetrists is from Juglans regia, and is probably identical. As supplied by Merck, it is in the form of a brownish powder, of a saline and slightly bitter taste, little soluble in water, freely in alcohol.

Juglandin possesses the virtues of the astringent aromatic bitters. It is a mild stimulant to the alimentary canal, laxative, in larger doses gently cathartic, causing no griping or subsequent weakness of the intestine (Felter and Lloyd). It closely resembles rhubarb in stimulating the gastrointestinal secretions but does not have the subsequent constipating action so markedly. The above authors recommend it in colorectitis, habitual constipation and other intestinal affections; atonic dyspepsia, indigestion with sourness and flatulence; tenesmic burning, fetid diarrheas and dysenteries, and intestinal indigestion with irritation; scrofula and chronic skin diseases with vesicles or pustules; as a cathartic in rheumatism and chronic respiratory affections; lumbago, intermittent and remittent fevers with abdominal congestion; murrain and yellow water of horses.

Specific Indications.—Chronic constipation, gastrointestinal irritability with sour eructations, flatulence and either diarrhea or constipation; diarrhea and dysentery with tenesmus and burning fetid discharges; torpid liver; chronic pustular or vesicular skin diseases freely discharging; eczema.

Ellingwood says it influences with great energy the liver, small intestines, colon and rectum, increasing the formation and flow of bile, and the activity of the intestinal glands. It closely resembles iridin. He considers juglandin valuable in duodenal catarrh, with torpid liver and jaundice, in small doses in dysentery and bilious diarrhea, and in intestinal diseases with irritability, hyperemia and tendency to inflammation; chronic constipation if dependent on defective elimination of bile, the stools clayey and dry; eczema, herpes circinatus, impetigo, pemphigus, rupia, prurigo, molluscum, lichen and chronic scaly affections; mucous irritations of throat, eruptions like scarlatina, *noli me tangere*, scrofulous glands, congestion and irritation of the respiratory and gastric mucosa; nursing sore mouth, mouth ulcers with constipation; used locally and internally for chronic ill-conditioned ulcers, stimulating waste and improving nutrition.

How much of the effects of this remedy as above described may be summed up in the remark that it clears out the fetid contents of the bowel, stimulates a healthier secretion of the alimentary fluids throughout, and thus puts a stop to the toxemia resulting from the absorption of poisons from the alimentary canal. The eclectics have made many true observations as to the uses of such remedies, but they seem to have totally failed to account for their effects, or to grasp the principle that explains their pathology, and the success of their therapeutics.

Laura suggests that juglandin is useful as a laxative in strumous cases, dyscrasic dyspepsias and other specific diatheses.

Van Renterghem found he required two to three centigrams twice a day—gr. 1-3 to 1-2—to produce a purgative effect. Besides its purgative qualities he credits juglandin with special value in scrofula, the syphilitic cachexia, the mercurial dyscrasia, chronic intestinal catarrh, and helminthiasis. Used after mercury it is certainly beneficial, without possessing any specific control over syphilis (Pearson). Even here it is the digestive difficulties that are remedied by juglandin and that constitute the indication for its employment (Posner). Droixhe counted on curing 75 percent of scrofulas with this agent; which acted mildly, with few relapses; the effects were slowly manifested, especially with non-suppurating glands;

the local effects of the leaves being more decided than the internal administration; especially did he urge it as the best treatment of scrofulous ophthalmias.

Van Renterghem advises doses of gr. 1-3 to j four to five times a day. It may be associated with santonin for worms, mercury for syphilis, or with other cathartics.

"It is in the extract from the leaves of the European walnut-tree," says J. Roussel, "that Luton, a distinguished professor of the school at Rheims, and author of some interesting therapeutic discoveries, found the most powerful aid against pulmonary and miliary tuberculosis. The effects of this preparation, he writes, are admirable; the fever is allayed, the tongue is cleaned, the appetite returns, and, in a word, the patient is born again to life. All the functions which were either suspended or perverted take on their habitual course. In the chest things improve from moment to moment; dyspnea ceases, pulmonary obstructions are dissipated, the râles become free and hurried, expectoration is without pain and ceases altogether. Let us add," says Roussel, "to be just, that it was the work of Negrier of Angiers, on the medicament in question (*Archives generales de medicine*, 1841-1844) that drew the attention of the learned professor of Rheims to it, only that the former never thought of treating anything else but strumous affections with that remedy, while the latter attacked with it the more formidable tuberculosis. We have, therefore, incontestable medical authority to conclude, that a dose of three, four or six grains daily of the extract of walnut is a most powerful remedy against chronic bronchitis."

From the above it is quite evident that Roussel, as well as our other confreres elsewhere, is totally ignorant of the experience of the dosimetric school with this juglandin, the active principle of the royal walnut (Juglans regia, Juglandaceæ).

Juglandin physiologically activates the appetite, favors digestion, while it is at the same time astringent and tonic. It is on this account that it is therapeutically indicated in the treatment of dyscrasic dyspepsias, scrofula and tuberculosis.

Juglandin is administered in milligram granules ten to twenty a day, or in centigram granules one to two a day.

Run through the works of the founder of the dosimetric school or those of his prominent disciples, Van Renterghem, Laura, Oliviera, Castro, Ferran, etc., and you will find invariably that juglandin is recommended as an antitubercle reconstructive. Ferran especially praises it as highly as Luton, considering it an excellent

remedy in that disease, which keeps the medical profession at present full of solicitude the world over." [I myself have used it the last fifteen years and was always glad that I had adopted it (Salivas).]

"The effects noticed by Luton I have often observed in my patients, and with patience and time I always had perfectly satisfactory results. I agree with what Negrier says in his lucid memoir on the 'Employment of the Walnut Preparation in all Scrofulous Affections at all Stages,' that one must have courage to persevere month after month, and even a whole year, to gain good results.

"I prefer the granules of juglandin to the extract of the walnut leaves, and I advise my patients to take one or two centigram granules of juglandin daily, and at the same time the compound antidiathetic granules, and all of these with an infusion of the dried walnut leaves. (This compound granule consists of strychnine arsenate, 1-2 milligram, helenin 1 centigr., and tannin 1 centig.) Rabuteau says that this infusion is almost as agreeable as tea, a fact of which many are ignorant. My patients feel themselves well in every respect, under this procedure of mine.

"It will be seen that the utilization of the physiologic and therapeutic properties of the dried leaves, or bark of the walnut tree in an organism tainted with scrofula or tuberculosis is not so rare as it would seem from what J. Roussel says. Dosimetrists make extensive use of it. I will add that it is a traditional remedy retained in many families, notably so in southern France. I speak of that region because I know what is going on there, having been born there and having lived there up to my twentieth year.

"The mothers of that region make their scrofulous or simply lymphatic children take a decoction of the dried walnut leaves every morning for months. Personally I had to submit in my early infancy to this prophylactic measure, and I certainly profited by it in common with my little comrades.

"I take advantage, therefore, of the occasion offered by J. Roussel, to urge a new juglandin upon the attention of those of my dosimetric (alkalometric) confreres who have lost sight of the remedy. I hope they will believe me. In juglandin, employed concurrently with the antidiathetic granules, and a hygienodietetic regimen, and continued, if necessary, for many months, they will find a powerful aid in combating a disease against which the practician feels himself absolutely disarmed, but wrongly so. And I repeat it to them with Negrier that they should not be discouraged, but persevere a long time, a very long time, and get final

success at this price. 'Genius is made of patience,' said a deep thinker, and the same may be said of the cure of tuberculosis.

"If compared with other remedies, even the most reputable ones, juglandin should seem to act more slowly, it has at least this advantage over them, that when used together with other appropriate remedies, juglandin acts surely. Let us not, therefore, demand of it what it cannot give, but let us know how to allow it all the time it needs to procure for us the certain benefits it can."

KOUSSEIN

Standard granules—gr. 1-67, Gm. .001; gr. 1-6, Gm. .01.

Koussein is a resin derived from Brayera anthelmintica, a tree of Abyssinia. It is yellowish white, partly crystalline, disagreeably bitter, almost insoluble in water, quite soluble in stronger alcohol and in ether, ammonia and caustic alkalies. Two alkaloids have been found in kousso, one of which is a dangerous paralyzant of the peripheral muscles and those of respiration, but neither has been studied closely. Kusotoxin also paralyzes the heart. It causes dyspnea, rapid breathing, salivation and vomiting. In large doses kousso causes diarrhea and increases the urine. It seems to be a general protoplasmic poison (Cushny). Given in pregnancy kousso is liable to cause abortion.

All varieties of tape worm and the lumbricoid also, are destroyed by this agent. Kuechenmeister found that they died in half an hour when placed in a milky infusion of kousso; in two or three hours in an albuminous mixture. The maceration it undergoes renders it difficult to detect the head of the worm.

Sollmann states that the active principle of kousso is kosotoxin, a non-nitrogenous neutral principle; aided by the two resins, coussin and cosin, and the volatile oils. Laura describes the official preparations as nauseous and repugnant, causing nausea, often vomiting, colics, vertigos, even true convulsions, especially in infants. Pelletierin gives rise to none of these and is a true anthelmintic. For infants especially Laura advocates koussein, given in small successive doses. Following the advice of Schmiedeberg he first gives a cathartic to diminish the contents of the bowels; and limits the patient to a milk diet for two days. Begin with a saline, follow with one of the quickly acting purgatives, that increase peristalsis; then give the tenicide.

Jack found that a dose of 1-2 ounce of kousso caused a sensation of emptiness of the stomach, slight nausea, fatigue and dislike of

work, then gurgling in the bowels, and after an hour and a half many copious stools, at first solid, then liquid. There was no headache nor vomiting, pains in the stomach or difficulty in urinating, symptoms often presented by those who have taken doses of six drams (Hasse, Petit).

Van Renterghem says koussein acts even against ascarides. He advises never to give a tenicide unless the sections of the worm have been passed and are recognized as such by the physicians. Of the granules containing gr. 1-6 each he gives an adult every quarter hour, beginning at 6 a. m., and after the fourth dose administers a dose of castor oil. This is to be repeated till the tenia has been expelled. For ascarides, in children under two years of age, he gives gr. 1-3 each of koussein and santonin, during the day. For older children give larger doses. Begin each day with an intestinal lavage with saline. Juglandin should be added if there are evidences of scrofula.

Somewhere we have read that in Abyssinia where tenias are considered a matter of course, kousso is only taken as a means of disciplining the parasite when he becomes troublesome, not with the intention of destroying him. In America the use of koussein has been almost entirely replaced by that of male fern.

LECITHIN

Standard tablet—gr. 1, Gm. .065.

In 1895, Danilewsky made the startling discovery that lecithin, administered to growing animals, was capable of stimulating their growth. He administered this substance to three young rabbits, all of the same litter, keeping three others as controls, that is, giving these no lecithin. He found that the animals treated with the lecithin grew nearly twice as fast as those that had not been so treated. This discovery created a tremendous sensation at the time and was largely responsible for the latter-day revival of organotherapy.

In the use of lecithin we have a true substitution treatment; for, by giving this substance, we supply something to the organism that is lacking in many morbid conditions. Its employment is indicated on the same grounds (in the conditions to be enumerated below), as the administration of thyroid preparations in myxedema and cretinism.

Though discovered many years ago, lecithin for a long time commanded only an academic interest. This was due to the fact that it could be manufactured only in very small quantities and by

a very complicated process, and that the chemists who experimented with this body were laboratory workers and not clinicians.

A number of socalled "lecithins" have been made from the yolk of eggs. It is claimed that these are therapeutically not so active as lecithin made from animal tissues; the explanation that can be ventured is that lecithin as found in the egg is really an inert storage body, not meant to be utilized until the chick embryo begins its life processes, whereas lecithin made from animal tissue (properly, as in Neuro-Lecithin, Abbott, from nervous tissue), represents a product that is living at the time the animal is killed, and does not die with it.

Lecithin is universally distributed throughout the organic world and is found wherever protoplasm is alive. It always occurs in nature combined with certain albumins, and in order that it may be properly assimilated must be isolated from its albuminoid combinations. If this were not necessary it would be a very simple matter to administer lecithin in the form of yolk of egg or of brain substance.

In administering lecithin, we supply phosphorus in true organic combination. It has been the aim of therapeutists for many years to find a phosphorus compound that is easily assimilated and properly retained by the tissues, the reason being that in all wasting diseases, in neurasthenia and nervous debility of all kinds, there is always a loss of organic phosphorus. It may be considered a clearly recognized postulate that unless this phosphorus is replaced the organism cannot perform its functions in a normal manner.

At first clinicians gave certain inorganic salts of phosphorus, such as sodium phosphate, and later the hypophosphite of sodium; then certain French physicians, recognizing that in lecithin the phosphorus is combined with glycerin, introduced the socalled glycerophosphates. All these have proved therapeutic failures and have been abandoned by conservative therapeutists.

In lecithin a phosphorus combination has at last been found that is readily assimilated and that can be used to supply phosphorus to starved nerve tissues whenever they cry for it.

Sollmann says that lecithin is advanced as a general nutritive tonic. It is claimed that it increases the weight and rate of growth in young animals, stimulating nutrition, and not as a nutrient, the proportion of red blood-corpuscles and the hemoglobin rising the mononuclear leucocytes increasing. The appetite and the fixation of nitrogen are improved, the urinary excretion of urea,

and of total nitrogen are raised, the acidity increased and the uric acid slightly lessened. These changes persist for five months, and then subside. The effect on nutrition also ceases. Large doses have not induced cholin toxemia as was feared. Lecithin is useless if improvement is not evident after ten days' administration. Lecithin is advised wherever there are faulty nutrition and growth, for artificially fed infants, for anemia, chlorosis, debility, convalescence, tuberculosis, tabes, neurasthenia, pancreatic diabetes, rickets, senility, and cachectic states; wherever the reconstructive forces need encouragement.

The salts of lecithin crystallize but the crystals are very unstable. It combines with platinum chloride, and forms a chloroplatinate which is sparingly soluble in alcohol, very soluble in ether and in chloroform, but the compound is unstable. It combines also with cadmium chloride. Sulphureted hydrogen precipitates all the metal from it and combines the lecithin in the state of an unstable lecithin chloride.

Lecithin dissolves in its own weight of hot alcohol, and of hot chloroform. This solubility will allow us to distinguish it from the hypophosphites that are soluble in alcohol and not in chloroform; and again from the nucleins that are insoluble in alkalies and also in sodium phosphate.

Danilewsky says: "There is no doubt that the division of the cell elements, their development, metamorphosis and differentiation, are intimately connected with the chemical changes which take place in the nuclear and protoplasmic substances of the cell. We have to assume a direct or indirect impelling influence on the morphologic course of the processes, either by substances which have already become integral parts of the protoplasm, their assimilation in it by external means being noticeable, or by the substances formed within the cells, owing to the chemical process proper of the living protoplasm.

"We have to assume this because the stimulating or organoplastic action of the nutritive proteic substances is quite limited. That hypothesis seems more probably true, which attributes such a bioplastic force to organic substances which do not, like those proteids, come from without, but to those which become nascent within the bioplasm itself owing to the chemical force proper to itself. Of the greatest interest in this connection are the phosphorated substances which are integral parts of the nucleus, viz., nuclein and lecithin. It can be assumed *a priori*, that they are very important for the energy of cell growth and multiplication."

Danilewsky relates one of his experiments illustrating the above assumption. In one of two vases with water in which he placed fertilized frog spawn, he added from one to one and a half Grams of lecithin. In two months after that he saw the tadpoles in the vase with lecithin to be half again as large as those in the control vase without lecithin. He also noticed that the water-cress which he put in the vases made from fifty to a hundred percent longer roots in the vase with lecithin than the cress in the control vase without the lecithin. This beautifully confirmed Hoppe-Seyler's contention, that chlorophyl is but a lecithin in which the fatty acids are replaced by the special chlorophanic acid. It also illustrates the happy dictum of Stoklasa: "Without phosphorus, no chlorophyl, without phosphorus no lecithin." It was further shown by experiments on young dogs and plants, that lecithin is a stimulant of growing tissues, and in animals especially the tissues of the blood-making organs, the spleen and the bone marrow.

When lecithin began to be administered therapeutically it was objected by some that if administered *per os* it is decomposed by the pancreatic juice, and it was thought best to give it hypodermically. But the answer is pertinent, that if it is decomposed it may again, like many other ingested remedies, be recomposed from the decomposed parts. But the fact stands unimpeached, that lecithin is not found excreted by either urine or feces, and it must, therefore, do its beneficial work just as the lecithin in the organism. Lecithin has also a marked influence on the nutrition which shows itself by a greater elaboration of nitrogen and fixation of phosphorus, and the augmentation of the animal's weight, and in this connection it is indifferent to the results, whether given hypodermically or *per os*. It was also shown that lecithin can be administered without ill-effects for many months.

It was questioned whether lecithin may not have an injurious fixing, or retaining effect on poisonous remedies, and experiments with strychnine and with potassium cyanide on animals and humans established the negative. Lecithin was shown to increase the resistance and volume of red corpuscles of the blood, etc.

The general testimony is in favor of lecithin in cases of debility, as a powerful restorer of the appetite and as an increaser of the bodily weight. Lancereaux reports two cases of pancreatic diabetes in an advanced stage of the disease, failing more and more every day in spite of all medications. On the administration of fifty centigrams (gr. 7 1-2) daily their emaciation ceased, they gained in weight rapidly, general condition ameliorated.

Another case he reports is that of a young man, eighteen years of age, affected with osseous tuberculosis, amyloid degeneration of the kidneys and abundant albuminuria, who took 0.3 (gr. 3 1-2) lecithin daily for fifteen days, and gained three kilograms (about seven pounds).

Another case was that of a child ten years old, very thin, having evening fevers and cough, who took Gram 0.2 (gr. 3) of lecithin daily and gained five and two-fifths pounds of weight. Another child with broncho-pneumonia, very thin, gained the same in weight on the same dose.

Huchard tried lecithin on chlorotics, dyspeptics, patients with gastric ulcer, and one case with Parkinson's disease (paralysis agitans), who after an attack of bronchitis was in a precarious condition. The general results in all these were the same, viz., increase of bodily weight, return of strength, and general improved condition.

Carriere gave lecithin to children in normal conditions and observed in all of them, compared with children who did not take the medicament, an increase of stature. There was an increase of the red corpuscles, the hematoblasts, and leucocytes. In the urine there was an increase of the urea; the nitrogen total also increased; the phosphoric acid first decreased and then became normal. There was no change in the sulphates.

Narbel of Lausanne tried lecithin on a number of children suffering from malnutrition to a degree which seemed desperate. He saw them under the influence of this remedy greatly improve in the functions of the alimentary canal: the stools decreased in number and their consistency increased and became normal; the appetite increased with the improved assimilation. Narbel gave the medicament hypodermically, a cubic centimeter every two days.

In tuberculous patients Gilbert and Fournir noticed from lecithin an increase of appetite and of bodily weight, a decrease of the cough and expectoration and of the bacilli in them.

Claude and Ali-Zaky say that while lecithin does not cut short tuberculosis directly, it yet modifies very happily the patient's appetite, increases his bodily weight perceptibly, the metabolism becomes active, and the elimination of phosphorus much less.

In the first and second stages of tuberculosis lecithin markedly diminishes the elimination of phosphorus and increases the bodily weight, but does not do these in the third stage of the disease.

The following points are a resume of recent experiences with lecithin:

1. Lecithin as an organic phosphorus body assists nutrition powerfully by constant diminution of the elimination of phosphorus from the body.

2. Lecithin is non-toxic, and perfectly assimilable.

3. The best form of administration is, perhaps, that of lecithinized milk.

4. Lecithin is a powerful bioplastic and morphogenous agent modifying importantly the organic changes of the organism.

5. Lecithin is indicated in all diseases where defective nutrition is a feature.

6. In tuberculosis lecithin must be regarded as a most valuable adjuvant, which acts in some specific way against the loss of the phosphates from the body.

Martell says that autointoxication of the nerve centers may cause complete loss of irritability, long before the supply of oxygen is exhausted. Certain poisons affect only certain definite parts of the nervous system, as morphine or strychnine, which affect the sensitive roots of the posterior horns only, while phenol affects only the motor cells of the anterior horns. It is not strange that when there is nerve exhaustion in consequence of certain metabolic conditions, and osmotic and electric tensions connected with these, the autointoxication should affect a definite portion of the nervous system. This explains the great variety of clinical aspects of neurasthenic diseases.

To this group of nerve-center diseases from over-irritation should be added the effects of heat, from insolation or direct radiation of a heat source, inducing an alteration in the thermic nerve centers. These no doubt depend on the loss of lecithin, for here, too, we have autointoxication. This is relieved by perspiration until this resource is exhausted. The chromatophile tigroid substance of the cells succumbs to chromatolysis, disappears and becomes scattered like dust in the protoplasm. Deeper-going changes occur in the nucleus and in the cell itself. Lecithin being an integral component of nerves and neurons, we must expect that with every loss of lecithin by these organs there will be a deficiency, first in these neurons, then in groups of neurons, lastly in organs electrically dependent upon these neurons. We have in the increased or diminished activity of an organ a means of judging of the biochemical energy of the nerve centers. A loss of lecithin in the central nervous apparatus will produce a loss of energy in the organs, according to the rate of loss of lecithin in this apparatus, which will manifest itself anatomically in degeneration. An excess

of work may bring on profound decay of the neurons. Waste products accumulate and a chemical irritation causes severe nutritive disturbance or inflammation of the nervous apparatus. The loss of lecithin then produces a transient or prolonged damage of the nerve centers, corresponding with an anatomicopathologic basis. There will be definite clinical aspects of disease.

We have therefore two clinical forms of spinal irritation, the hyperesthetic and the depressive. Since the change of electric and osmotic tension induced by abnormal metabolic processes need not attack the entire organ, we see in consequence of autointoxication in one case an affection of the cervical cord, in another a disorder of the lumbar enlargement. This may be shown by the pain on pressure in the irritated area. After physical excess connected with the cardiac and pulmonary activity we will find the pain in the upper cervical cord; after excesses *in Baccho et Venere*, when the abdominal organs are overtaxed, the pain will be found in the lumbar cord. If these disturbances are due to a deficiency of lecithin, as Danilewsky maintains, we are right in expecting relief by supplying this deficiency. We thus supply neurogenic material to the apparatus of the centers and restore them for their work of innervation and electric supply.

Martell has experimented with lecithin since 1895, obtaining it from the parts of the animal organism which are richest in phosphorus, namely the brain and cord. The remarkable fact came to light that there was a difference in the biologic behavior of lecithin accordingly as it was derived from the brain, medulla, cervical or lumbar cords. That from the brain he found effective in cerebral spasm in little children, not in tubercular forms. Sleep was induced by cerebro-lecithin in patients who had resisted morphine up to 1-3 grain. The surprising cessation of spasms in these cases of children suggested its use in psychic alterations. He used it with a woman suffering from cerebral neurasthenia, with periodic psychic depression. After some days the agitation ceased completely and there was nearly always a beneficently refreshing sleep.

A veterinary surgeon used hypodermics of lecithin in cerebrospinal meningitis of horses, with success.

Martell thought the application of lecithin would do away with much of the use of direct narcotics. Lecithin obtained from the medulla and the cervical cord has a direct vasomotor effect on incipient and established cardiac diseases. In six cases of palpitation with cardiac neuroses, lecithin from the medulla quieted excessive activity and after four or six weeks' treatment the heart-action was

normal. In two cases of mitral insufficiency eight weeks' treatment restored the heart to normal. In three cases of acute heart-weakness with asthma and commencing pulmonary edema, there was an abatement of cardiac oppression after twenty-four hours' treatment, when sleep and perspiration occurred. In a case of acute cardiac dilatation in a farmer, aged 56 years, who had overworked himself in the harvest field, the heart returned to its normal dimensions after eight weeks of treatment. In an organic heart-lesion with stenosis of the left ostium, ascites, scrotal edema, and anasarca of the leg, in a patient 58 years of age, lecithin proved a most efficient diuretic.

Lecithin obtained from the lumbar cord showed an eminent influence over the abdominal organs. In nervous gastralgia it stopped the spasms and vomiting, obviating the necessity of stomach lavage. In acute vomiting from a psychic trauma in a man 72 years old, the vomiting and diarrhea ceased after three doses of lecithin, the patient breaking out in profuse perspiration. In two cases of acute intestinal atony with obstinate constipation there was complete restoration of intestinal peristaltic function after three weeks' treatment with lecithin.

In a case of retention and dribbling of urine improvement followed eight days' treatment. In four weeks the patient was cured. Lecithin showed its tonic power in masculine impotence. A man, 42 years old, had been impotent for one year; the sexual functions were perfectly restored, his bodily weight being diminished. This brings up two cases of obesity; in one twenty pounds were lost in twelve weeks' treatment; in another fourteen and one-half pounds in eight weeks. This lecithin proved very effective in two cases of sluggish parturient pains, one of dysmenorrhea, and one of commencing vaginal prolapse.

Finally, Martell mentions lecithin as a powerful tonic in lingering weakness of the nervous and muscular tissues after infectious disease. Convalescence from rheumatism was essentially shortened.

Colombe gives as indications of lecithin: Anemia and chlorosis, disturbed nutrition in tuberculosis, diabetes, rachitis, gastric ulcer, cancer, tubercular cachexia and neurasthenia. This indicates the wide range of its applications.

Martell concludes as follows: "The treatment with lecithin promises to conquer for itself a dominant place in therapy, and I believe this especially true in respect to animal lecithin." He further mentions its use in uric-acid diathesis, hemorrhoids, etc.

Serono reports that his experiments demonstrated the usefulness of lecithin in dyspepsia, neurasthenia, anemia with diarrhea, hysteria, tuberculosis in the first and second stages, chlorosis, diabetes, nephritis, and chronic enteritis. He presents the following summing of his observations: Increase of bodily weight in seven days two to five kilograms, after twelve days four to five kilograms; lively appetite; increase of blood's red corpuscles; general improvement of the health. These results were verified by other Italian physicians, especially in neurasthenia. The same good results followed the administration of lecithin given by the stomach, as hypodermically. In the latter case it is dissolved in sterilized oil or in physiologic salt solution. The dose given is from two to three centigrams. By the mouth the dose may be increased to six centigrams, as there is no danger. It has not been shown that larger doses are advisable.

Gautier maintains that in nervous activity it is the burning up of lecithin that forms the main source of the increased excretion of phosphorus. Since mental and physical work go hand in hand with decomposition of the natural phosphorus, we have in lecithin an agent by which to restore the equilibrium which becomes disturbed in the complexes of the neurons. The disturbances produced in the neurons by irritation manifest themselves, if not equilibrated, in the sense of tire and exhaustion. In both cases we have conditions of intoxication. In fatigue there is an excess of carbonic acid and other metabolic products soluble in water, especially of lactic acid. Exhaustion takes place when the oxygen in the neurons has been consumed. The reduction of intraorganic oxidation plays here a very important part. The lactic and other acids appear during strong muscular and nervous incitation and disappear if it does not last long. These may saturate the tissues and, not being neutralized or oxidized by the blood current, produce an acid intoxication.

Buchholz states that a patient suffered with neuralgic pains in the extremities, back of the neck and head, with girdle pains, staggering gait, and loss of reflexes. These symptoms so increased that for three years he was unfit for manual labor. He was put on lecithin, and Crede's metallic silver ointment rubbed into the back and spine, with attention to excretion. Under this treatment the disease not only stopped progress but the patient improved. Several times he ran out of lecithin, when a renewal of the disease would be noted. At the last report the patient could walk fairly well, the pains had diminished, and he was able to do a part of his work; he slept better, had a better appetite and better color.

In another case, a man of forty, had periodic spells with difficulty of the mitral valve. He was given cactus and lecithin for two months, with attention to secretion and excretion. The trouble disappeared and has not reappeared.

LEPTANDRIN

Standard granule—gr. 1-6, Gm. .01.

Leptandrin is a resin from Leptandra Virginica, or Culver's root. Lloyd states that the ordinary leptandrin is inert, the hydro-alcoholic extract alone carrying with it the virtues of the plant.

Lloyd says that leptandra acts upon the stomach, liver and intestines; the fresh root causing dangerous catharsis, emesis, dysentery, vertigo and in pregnant women miscarriage. On drying it becomes a safe and reliable cholagog, laxative and cathartic. In small doses it does not physic but gently stimulates the liver and the functional activity of the whole intestinal appendages. It favors normal intestinal excretion and improves digestion. Scudder used it as a gastrointestinal tonic, for feeble circulation with stasis. It acts well in intestinal atony, hepatic torpor, the early stages of fevers and dysentery, and in chronic dysentery and enteritis with dizziness, cold extremities, headache, abdominal and hepatic pain with mental depression. Stimulating the glandular system to activity it is useful in chronic catarrhs; for indigestion with deficient secretion adding podophyllin, for acholic stools even if there is diarrhea; dyspepsia with frontal headache, yellow tongue, nausea, jaundice; for gastric atony combining with hydrastis; for diarrhea with passage of undigested food, inactive liver, dull abdominal pain, stools clayey; in diarrhea of dentition; for jaundice with tender liver add rhubarb; biliousness; for acute hepatitis add a diaphoretic; give an occasional dose in chronic hepatitis; after passage of biliary calculi, with hydrastis to alter the conditions giving rise to the concretions; for jaundice add dioscorea, chionanthus or chelidonium; in formative stages of fevers, especially bilious, it often checks the morbid process; in typhoid in malarial districts; in malaria after quinine has broken the chills; dropsy, hydrocephalus, ascites with congested liver and despondency; to remove fluid and prevent accumulation.

Specific Indications.—Drowsiness, dizziness and mental depression with tenderness and heavy pain in liver; tongue white, skin yellow, bitter taste, cold extremities, nausea, dull frontal headache, thirst with inability to drink, restlessness with insomnia;

diarrhea with half-digested passages or clayey stools, feeble portal circulation with lassitude and mental depression.

As a purgative leptandrin should be given in doses of gr. 1-6 every hour, or six times this at once. For its action on the chronic affections above enumerated give gr. 1-6 every two hours, or a grain at bedtime. It should not be forgotten that the best effects of this remedy are obtained without obvious catharsis.

LOBELIN

Standard granule—gr. 1-12, Gm. .005.

Lobelin is a concentration from Lobelia inflata, Indian tobacco. Lobelia contains an alkaloid, lobeline, isolated by Procter, a liquid, described by King as acrid, irritant and unstable. The salts are stable. It is soluble in alcohol, chloroform, and somewhat in water. Lloyd also found a non-crystallizable body to which he gave the name of inflatin. A fixed oil is also extracted from the seeds, which contains the virtues of the plant.

Lobeline forms crystallizable salts. Eudros obtained a second alkaloid, lobelacrine, occurring in warty brownish masses. The latter has never been tested therapeutically. To it Laura attributes the acridity of the lobelia preparations, and he insists on the necessity of securing lobeline absolutely free from this acrid principle. He blames lobelacrine with the excessive gastrointestinal irritation caused by moderate doses of lobelia as well as with the circulatory and respiratory disorders and general depression of large doses. In minute doses lobeline is a sedative and a vital incitant. In massive, excessive doses it is a depressor of the vasomotor centers.

In successive small doses it augments the action of the heart, increases the pressure of the arterial system, excites the spinal centers and the peripheral nerves, moderating excessive waste.

Felter and Lloyd say that lobeline is so quick an emetic that it is impossible to poison with it. A drop of an alcoholic solution on a man's tongue caused instantaneous vomiting. Death in a very prostrate person might result from the repeated vomiting but not from the direct action of lobelia. When the drug is chewed it causes an acrid, pungent sensation, slight nausea, warmth and distention along the esophagus and stomach, the salivary and buccal glands secreting freely; then epigastric depression, profound nausea and if the dose is large enough, severe and thorough emesis. Profuse perspiration and profound depression attend. The muscles are relaxed, and a period of languor follows. The depression is very

short, and immediately followed by a sense of extreme satisfaction and repose. The mental powers are unusually acute. The circulation is weakened by large and strengthened by small doses. The bronchial secretions are increased. If emesis does not occur, purging does. If death results, it is from respiratory paralysis.

Lobelia is nauseant, emetic, expectorant, relaxant, antispasmodic, diaphoretic, sialagog, sedative, occasionally cathartic, diuretic, and astringent. It is in no sense a narcotic. Temporarily depressing, its beneficial after-effects make it preferred as an emetic to all others. It is safer and more effective when combined with ipecac. It is used in the forming stage of fevers, with sluggishness and heavily-coated tongue; in chronic diseases to arouse the system from atony. As an emetic give small doses in warm water rapidly repeated. Spasmodic movement is incompatible with nervous and muscular relaxation. Give nauseant doses for chorea, tetanus, children's worm fits, hysteric and infantile convulsions, epileptiform and other convulsions. It is the remedy for rigid os uteri, relaxing the perineum also; best for a thick, doughy os (gelsemium for thin knife edge); intestinal obstructions, strangulated hernia, intussusception, fecal impaction; asthmatic paroxysms, spasmodic croup, whooping-cough; strychnine poisoning; as a sympathetic stimulant, it improves the innervation of parts supplied by the pneumogastric and sympathetic; it is useful in indigestion, dyspepsia, gastric sick headache, qualmishness and nausea, intestinal atony and habitual constipation, with podophyllin for costiveness; it increases peristalsis, small doses relieve infantile colic; for angina pectoris, cardiac neuralgia and pulmonary apoplexy it is *the* drug; best remedy for markedly slow pulse-wave, with precordial oppression, thoracic pain, difficult breathing, soreness in chest, nausea, tongue heavily coated at base, and fulness of tissue; cardiac congestion; its great value is in respiratory affections, spasmodic asthma, whooping-cough, congestions, pleurisy, acute pneumonia, congestive, oppressed breathing, all chronic sore throats especially ulcerated, chronic pneumonia, bronchitis and laryngitis, asthenic laryngitis of children, dry hard and barking chronic catarrhs, coughs and colds, all respiratory irritations with congestion or oppression, the full oppressed or small feeble pulse with oppression anywhere in the chest, accumulated secretions and loud mucous rales; retrocession of eruptions, scarlatina and measles with tardy eruption, rhus poisoning, locally in many superficial inflammations and in erysipelas.

Specific Indications.—Full, labored, doughy pulse, blood moves with difficulty; heavy, sore oppressive chest pain; angina pectoris, cardiac neuralgia, pulmonary apoplexy; mucus accumulation in bronchi, convulsive movements, rigid muscles and os uteri with thick doughy edges, rigid perineum or vaginal walls, nausea and sick headache, as emetic for tongue heavily coated at the base.

Ellingwood places lobelia first in his list of agents acting upon the respiratory tract. He terms it a nerve depressant of great power. It is a specific for irritable, spasmodic and oppressed breathing; threatened spasm with exalted nerve action; high nerve tension with great restlessness and excitability, flushed face and contracted pupils; it affects children less than adults; for eclampsia and the spasms of hydrophobia, etc. He employs lobelia frequently in combination with capsicum.

The foregoing is the account given by the leading authorities in the eclectic school of this remarkable remedy that has held the first place with them for nearly a century, since Thompson introduced it.

Properly applied, lobeline occupies a wide field among the spasmodic affections, as a remedy for eclampsia, chorea, epilepsy, and according to some, for tetanus itself. Laura employs it with advantage to suppress the paroxysms of asthma, of any form, and as a symptomatic medicament to prevent its violent development. In this disease Ruatta pronounced lobeline one of our most powerful medicaments, while Fournier found it very useful in the cardiac nervous form and also in that dependent on aortic valvular disease. Here the asthmatic paroxysm may be the precursor of the development of graver conditions, even while as yet no valvular murmur is perceptible.

In cardiac asthmas we may associate lobeline with digitalin and strychnine, the latter being the most active remedy in the treatment of asthma, essential or nervous.

Lobeline also renders marvelous services when associated with the ordinary modifiers of whooping-cough, bronchitis, and spasmodic catarrhs, especially chronic bronchial catarrhs. Here it is well to add calx sulphurata, "that very precious modifier of all moist forms of mucous catarrh, not excluding specific forms; also employing antimony (Laura.) In strangulated hernia, invagination and retention of feces, Ruatta recommends this remedy in place of the dangerous infusion of tobacco. Laura confirms this application of lobeline.

Lobeline is usually administered by the mouth, but if desired, the granules may be dissolved and given in enemas, instead of the uncertain infusion. The dose varies with the need. In very grave and urgent cases we may give two granules, each gr. 1-134, every few minutes. Children display a remarkable tolerance for lobeline. After ascertaining the individual tolerance we may proceed boldly, watching the effect upon the heart—a precious index. As a rule lobeline should be administered in association with the alkaloidal remedies that specially incite and sustain the cardiac energy and vitality.

In the foregoing Laura has admirably depicted the value of lobeline as an antispasmodic. This, however, is but one of the uses of this valuable product of American materia medica. In all the mucous or catarrhal affections lobeline is applicable, whenever it is desirable to increase or loosen the secretion. This applies to the early hyperemic stages, when lobeline relaxes the vascular tension and soothes irritation, by promoting the free secretion that depletes the tense, swollen inflammatory area. It also applies to atrophic forms, dry, chronic catarrhs, as by it the remaining muciparous glands are incited to a healthy activity and greater comfort ensues. By stimulating the absorbents also, the debris remaining after the subsidence of the acute morbid process is carried away more rapidly, and certainly, and a healthy condition is more quickly restored. In the moderate doses alone proper, there is nothing debilitating in this action of lobeline, and the assertions of many clinicians who are practically familiar with the operation of this remedy, that it really enhances the vital functions and consequently acts as a tonic, are evidently based on correct observations. Anything that removes encumbering debris and restores normal activity of function is essentially restorative, even if waste is thereby increased. When the grain is shelled out we need not hold on to the husks.

Whenever a nauseant relaxant is really indicated, in catarrhal croup, bronchitis and other acute respiratory catarrhs, lobeline ranks with emetine, but is stronger and acts more speedily. Here the granules should be given in warm water, one every five minutes until effect. A nice choice may be made of lobeline for the lusty, emetine for the feeble, and apomorphine when freer secretion is desired without any nausea whatever. Lobeline is also a useful ingredient of laxative combinations when costiveness is to be obviated.

There is no better remedy with which to practise and attain the art of exact dosage. Give just enough lobeline for costiveness,

and the effect is only perceptible in the removal of the difficulty and the establishment of normal, healthy, alvine discharges. The patient is not to be trusted with the judgment—he wants results that are more decided, and is likely to declare there has been no effect. Overaction exhausts vital irritability. Give exactly enough and no more, and in a short time the result may be secured from smaller and from constantly decreasing doses, until no medicine whatever is needed. Very few physicians, or patients, possess the skill and exercise the patient watchfulness necessary to secure such results; consequently to the majority the virtues of lobeline are unknown—and discredited.

In asthma Ruatta pronounced lobeline one of the most powerful medicaments in the materia medica, and Fournier found it very useful in cardiac nervous asthma, and in that form accompanying aortic lesions. Here asthma may be the precursor of the gravest exacerbations of the lesion. Laura also advocates this remedy in whooping-cough, catarrhs, spasmodic bronchitis, etc. Ruatta substituted lobeline for tobacco in relaxing strangulated hernias, invaginations and retention of feces.

Cushny says lobeline increases reflex irritability; accelerating the respiration by stimulating the centers in the cord and medulla. It resembles nicotine in some respects. The blood pressure at first falls, but soon rises above normal. The respirations are faster, deeper and stronger. He limits its therapeutic use to nervous asthma.

Cornet found lobeline sulphate effective in the spasmodic cough of phthisis, and giving almost magical results in the various forms of croup. It also proved useful in chronic bronchitis, asthma, and the convulsive cough of pertussis.

One general indication for its use seems to have been too slightly advocated—that of loosening secretions in catarrhal maladies of the dry type.

The dose of lobelin is from gr. 1-12 to 1-2, repeated every five minutes to thirty, always given dissolved in hot water, as the granules are apt to pass through the bowels unchanged. Thus given in smaller doses, lobelin has proved quite effective in costiveness of very young infants.

LYCOPIN

Standard granule—gr. 1-6, Gm. .01.

Lycopin is a concentration from Lycopus Virginicus, or bugle weed.

It is claimed that lycopin acts as a specific vasoconstrictor for the pulmonary circulation. The claim has not been proved or disproved. There must have been a reason for this assertion, and the observation if verified is of enough importance to justify full and impartial investigation.

Felter and Lloyd term lycopus a certain sedative, mild narcotic, sub-astringent and tonic. Its sedation is best shown when the heart is tumultuous and pulse rapid with evident lack of cardiac power. It is useful in the late stages of acute affections with great debility and in chronic cases with fast pulse. It acts somewhat like digitalis, controlling excessive vascular excitement and lessening exalted organic action. It improves the appetite, reestablishes normal secretion, and improves blood making and nutrition. It is a remedy for morbid vigilance and insomnia, painful and distressing indigestion, to purify the blood for old ulcers, diabetes mellitus, albuminuria with rapid irritated pulse; frequent small hemorrhages, such as hemoptysis, epistaxis, hematuria, uterine and intestinal hemorrhages; dysentery and diarrhea, especially of phthisis, a soothing remedy in gastritis and enteritis and the gastric and intestinal affections of drunkards and of malaria; inflammations of the heart, palpitation, with irritability and irregularity, dyspnea and oppression; dilated and hypertrophied hearts, relieving the suffering and anxiety; exophthalmic goiter; acute and still more in chronic lung ails, a gentle sedative and tonic, for irritation and cough with tendency to hemorrhage, relieves cough of chronic bronchitis, pneumonia and consumption, giving rest and quieting pain, acute catarrhs; for pulmonary hemorrhage with cinnamon and ipecac the best of remedies.

Specific Indications.—Vascular excitement, small hemorrhages from determination of blood to lungs, kidneys or gastrointestinal organs; albuminuria with fast pulse; debilitating chronic cough with free sputa; wakefulness and morbid vigilance with too active circulation; fast pulse with high fever, and in tuberculosis.

Ellingwood looks for the specific effects of lycopus in heart affections with irritability and irregularity, dyspnea and oppression. It has succeeded in incipient phthisis, and hemoptysis; high fever of typhoid; it promotes digestion and invigorates the appetite.

Laura limits his applications of lycopin to feebleness of the gastric or intestinal functions, employing this agent as an antidyspeptic, digestive and excitant of peristaltic movement.

The dose of lycopin is from gr. 1-2 to 2 before each meal and at bedtime.

MACROTIN

Standard granule—gr. 1-6, Gm. .01.

Macrotin is a resinoid from Cimicifuga racemosa, bugle weed, rattle weed, or black cohosh.

Shoemaker says that cimicifuga in small doses stimulates the digestion, increasing the gastrointestinal secretions. It also increases the bronchial mucus and the urine, and strengthens the heart. The effect on the circulation resembles that of digitalin but is less powerful. Brunton styles it a succedaneum for ergot. Full doses slow the pulse and increase its force, raise vascular tension and stimulate contractions of the uterus. It lowers the reflex excitability of the cord, and dilates the pupils. Dimness of vision, vertigo, intense headache, nausea and vomiting, result from too large doses. Hypnotic effects have been reported, with relief from pain and spasm. Death may be caused by paralysis of respiration.

Lloyd says cimicifuga acts also upon the skin, imparting its earthy odor to the urine; small doses given hourly produce symptoms closely simulating those of delirium tremens; green tea is said to counteract the narcotic effects; cimicifuga increases the menstrual flow and possibly the venereal appetite.

Felter and Lloyd credit this remedy with decided values in rheumatism and neuralgia; muscular rheumatism, lumbago, torticollis, acute non-spinal pains such as gastralgia, enteralgia, tenesmus of bladder, pleurodynia, mediastinal pain, orbital and aural pains, eye strain with affection of ocular muscles; acute conjunctivitis; rheumatoid dyspepsias, with dull pain and tendency to metastasis, worse on taking food or drink, stomach walls feeling as if contracting on a hard substance, with rheumatic history; atony of reproductive tract, pains from imperfect menstruation, suppressed and especially non-established menses; it is unsurpassed in dysmenorrhea; best in irritation and congestion of uterus and appendages, with tensive dragging pains, like rheumatism; if despondent and chilly add pulsatilla, especially in anemics; if opposite, add gelsemium; for reflex side-aches of virgins, mastitis and mastodynia; uterine rheumatism and leucorrhea; sterility from uterine atony, reflex mammary pains during gestation, ovaralgia, neuralgia, orchialgia and aching prostate, and as a tonic in spermatorrhea; it excels ergot in parturition by producing natural pains, an excellent *partus praeparator* if given for some weeks previous to confinement, dissipating false pains and strengthening true ones, the best remedy for after-pains and allays the nervous excitement following labor;

for nervous cases, useful in chorea, best when menses are deficient, as an antispasmodic in hysteria, epilepsy due to amenorrhea, asthma, periodic convulsions, nervous excitability, whooping-cough, delirium tremens and other spasms; headache from cold or congestion; neuralgia, dysmenorrhea or influenza; in phthisis lessens cough, soothes pain, especially subscapular aching, lessens secretion and allays nervousness; malarial fevers are benefited by its tonic power; for rheumatic fever add aconite or veratrum; prompt and decisive in cerebral complications of eruptive fevers, especially in children, and in simple fevers; lessens the force and frequency of the pulse, soothes pain, allays irritability and lessens cerebral irritability and the tendency to congestion; in fevers, especially exanthemata, it often causes diaphoresis and diuresis, controls pain like the boneache of smallpox, renders the attack milder, relieves the headache and backache preceding the eruption, and has been thought prophylactic against smallpox; has a tonic influence over serous and mucous tissues, and is a superior remedy in their chronic maladies; add alkalies for acidity of stomach; often promptly relieves pains that have existed long; locally it is applied for neuritis, neuralgia, tic, spinal inflammation, periodic cephalic pain, ovaritis, spasms of the broad ligaments, rheumatism, "crick" in the back or side, ocular inflammations and old ulcers. Preparations from recently dried roots are preferred; in phthisis, cough, acute rheumatism, neuralgia, scrofula, phlegmasia dolens, amenorrhea, dysmenorrhea, leucorrhea and other uterine affections, the alcoholic preparations are urged alone.

Specific Indications—Muscular pains; uterine pains with tenderness, false pains, irregular pains, uterine rheumatism, dysmenorrhea; as an antirheumatic when pulse is open, pain paroxysmal, skin not dry and constricted (Scudder). To these add soreness, dragging pains in hips and loins, rheumatoid muscular pains and dyspepsia, chorea with absence of menses.

Ellingwood says an overdose is promptly signalled by the appearance of the characteristic headache, of bursting, tearing character, with injected conjunctivæ and flushed face, which abate when the remedy is suspended. He considers muscular aching the specific indication for cimicifuga. It is the remedy for hysteria with flushed face and hot head, restless nervous excitement and general muscular aching. He also gives it for angina pectoris, functional irregularity of the heart, cough of excessive nervous irritation, reflex, irritable or of acute bronchitis; lithemia, sciatica, dysmenorrhea and amenorrhea with aconite if from sudden cold,

pulsatilla if from nervous shock or functional irregularity of long standing, helonias if with weight and dragging in lower abdomen, and in all these it is better if leucorrhea is present. It is useful in male gonorrhea with aching in bladder and kidneys; with aconite, gelsemium, or hydrangea.

Shoemaker recommends cimicifuga in the menstrual disorders of young girls at puberty. Simpson used it for hypochondria and melancholy, and Ringer in rheumatoid arthritis. In weak and fatty heart Shoemaker pronounces it safer than digitalis.

Lloyd, who never has a good word for the older eclectic resinoids, prefers the fluid preparations; but Ellingwood says cimicifugin, or macrotin, fully represents the remedial virtues of the plant.

I have used preparations of macrotis for many years in the treatment of chorea, and frankly look upon it as the best-known remedy in this affection and one far superior to arsenic. It is best to begin with small doses, say gr. 1-6 of macrotin, repeated every one to three hours, and gradually increase until full tolerance, or until the vascular tension is normal. As the pulse is steadied the nervous perturbation subsides, and the patient appears better able to control his muscles. It is better to employ cathartics and the powerful sedatives in the early stages, such as cicutine and gelseminine, reserving macrotin for the decline of the attack. Thus employed it is very effective.

Many years ago cimicifuga was recommended enthusiastically as a remedy for pulmonary tuberculosis. Speaking of this, Stillé suggested that the cases reported as cured were probably chronic bronchitis. We know now that very many cases of true tuberculous consumption are really cured, nevertheless if cimicifuga can cure chronic bronchitis, it is of scarcely less importance than if the cases were truly tuberculous. Chronic bronchitis is not so readily cured. This is one of the remedies which has been established universally in the affections of the eclectics, the regular profession having made but little use of it. Probably this is because the preparations under which it has been presented are unworthy of confidence. Macrotin is accurate and effective, especially when pushed to full effect, by small and rapidly-repeated doses.

The dose of macrotin is from gr. 1-6 to 1 every hour in acute or painful affections till relief or the headache described by Ellingwood, or nausea, results. In chronic maladies the dose should be thus ascertained and it may then be so distributed that four daily doses are taken, one before each meal and one at bedtime.

MANGANESE

Standard granules (the arsenate)—gr. 1-67, Gm. .001; gr. 1-6, Gm. .01.

Manganese presents close analogies to iron, with which is it usually found associated in nature. Vauquelin discovered it in the hair; Bley and others in biliary and renal calculi; Wurzer in the blood; Petrequin in laudable pus; Jahn in the urine of a diabetic horse, and Sprengel and Bibra in that of a beef. More recently it has been found by Turner in the urine of a man. But many have failed to demonstrate it in the red blood globules, nor does it form an integral constituent of hemoglobin. Its existence in the red globules, many times affirmed, is considered doubtful by Gautier (Rabuteau).

The detection of a minute trace of manganese in the blood has led some to proclaim a manganese-anemia, as well as an iron-anemia. Hannon distinguished both, but Petrequin asserted that both iron and manganese were deficient in all chloroses. He therefore considered both essential in the treatment of chlorosis, but said that the ordinary martial preparations all contained manganese. This, however, was denied by Trousseau and Pidoux, and later by Rabuteau. The experiments of the latter, confirmed by Hayem, showed that instead of being hematogenous like iron, manganese actually diminished the red blood globules.

Gubler ranked manganese with iron as a constituent of the blood, and its salts as tonic reconstituents, pronouncing this metal a general and local stimulant, in all respects closely resembling iron.

Potain recommended manganese when in chlorosis iron was not well borne, a not infrequent condition; also when iron proved too stimulating, as with persons predisposed to tuberculosis. Before his time Trousseau had forcibly insisted on the danger of iron in these cases, where it is apt to induce hemorrhages from the bronchi. Potain affirmed that manganese surely provoked the formation of red cells. He described a case of leucocythemia, so marked that there was one white cell for each red one, the patient being unable to take iron, in which, after a month's treatment with manganese, the normal proportion was re-established. It is unfortunate that manganese is nearly always administered with iron, so that it is impossible to distinguish the value of the former.

Cahn's studies of manganese may be thus summarized: Introduced directly into the blood it is not incorporated in the red cells. It is reabsorbed and transported to the parenchymatous organs, and eliminated mainly by the intestinal mucosa, and passes out with the feces. Reabsorption by healthy intestinal mucosa does not occur.

Overdoses cause toxic symptoms, especially when given intravenously. Seven decigrams (10 grains) of the sulphate injected into the veins of a small dog killed it. Four Grams (one dram) by the stomach, killed a rabbit. In a bitch Rabuteau saw an intravenous injection of the lactate, two grains, cause trismus, opisthotonos, and death—all on the following day. But intravenous injections of iron are as toxic as those of arsenic, so that this furnishes no light on the gastric administration of manganese.

If the organism of man reacts like that of the dog, a subcutaneous injection of five decigrams (gr. 7 1-2) should kill an adult man within twenty-four hours.

Massive doses given by the mouth cause gastrointestinal catarrh, all the drug being absorbed, and principally eliminated by the kidneys. In animals, toxic doses of manganese cause vomiting, diarrhea, paralysis, tetanic spasms, exophthalmos, jaundice, somnolence, diminution of motility and sensation, and abolition of reflex irritability quickly followed by death from paralysis of the heart. The vasomotor center is paralyzed before the heart. The urine contains biliary coloring matter, hyaline casts, albumin and leucocytes. In chronic toxemia from manganese the jaundice is very grave.

Van Renterghem describes a case of poisoning by manganese in man. The workmen who grind manganese are subject to paralysis of the muscles of the extremities and of phonation; sometimes permanently, some not cured for years. Autopsies of animals killed by manganese show gastroenteritis, and inflammation of the spleen, liver and heart. The inflamed bowel is stained with bile. Chronic poisoning causes disease of the renal tissues.

The black oxide of manganese, in doses of 3 to 6 grains, is employed for acidity and waterbrash. Mix 20 grains with a dram of magnesia in a glass of water and let the patient take a small swallow every five minutes till relieved. This is often very effective. Gubler also gave this salt of manganese for chlorosis, anemia, scurvy and cachexias, the daily dose being 7 1-2 grains.

Manganese carbonate is employed in the same affections and in the same doses (Gubler). Manganese sulphate is a caustic solvent like potash and soda, and does not produce insoluble combinations with animal matter like iron (Mitscherlich). In the stomach it acts like the caustic alkalies mentioned, causing fatal erosions. It has been employed as a purgative cholagog, in doses of 4 to 7 1-2 grains a day, for torpid liver, jaundice and gout. Locally it has been applied as an ointment—one part to eight of lard—for neuralgias,

buboes, and to dissipate the residues from rheumatic and other arthrites. Manganese arsenate has been used to some extent by the French dosimetrists. It may have some advantages over iron arsenate in the way of solubility.

The most important item in the foregoing is the use of manganese in leucocythemia. The arsenate might be tested here, in doses of gr. 1-67 to gr. 1-6, several times a day.

Whether potassium permanganate is to be treated therapeutically as manganese or as an agent *sui generis*, is uncertain. Very important results have followed its employment, which do not harmonize with any as yet reported from any other preparation in which manganese enters. The permanganate was introduced as a remedy for amenorrhea many years ago, and acquired considerable repute; though Leffmann and others showed that the salt was decomposed the moment it entered the stomach. It is much more irritant than any ordinary preparation, and doses of gr. 1-4 every hour soon induce nausea.

The writer has found the black oxide of manganese decidedly active as an emmenagog.

Some years ago a Chicago physician began the use of the permanganate as a remedy for tuberculous phthisis, on account of its supposed "oxidizing" qualities. He reported that in every case the patients improved so decidedly that he looked for a cure, when they were suddenly seized with bronchial hemorrhages, usually fatal. The disposition to hemorrhage seemed very decided, and invariable when this salt was pushed to full dosage.

This indicates caution in the use of manganese, especially of the permanganate of potassium, in persons predisposed to tuberculosis, or to bronchial or other forms of hemorrhage. But a drug with such decided qualities should prove of therapeutic value when properly directed. As a remedy for amenorrhea the writer has frequently administered it with satisfactory results. The dose of gr. 1-4 every two to three hours, began two days before the flow is due and continued for a week, rarely fails to induce the discharge when the patient has the blood to spare. Whether it is effective or safe during pregnancy the writer has no knowledge—he has never given any emmenagog until certain that pregnancy was not present.

Quite recently a case came to the knowledge of the writer, where potassium permanganate was administered for amenorrhea, the woman not being pregnant, but feeble from digestive failure and excessive grief, for the loss of a child. Half a grain was administered every two hours for five days, when the stomach began

to reject the drug; it was continued, the physician not being in attendance, and the vomiting assumed the incessant character of gastritis. The secretion of urine almost ceased. The pulse became weak, and the whole aspect of the case quite threatening. Not a trace of effect upon the menstrual flow was at any time manifest; the woman being quite anemic. Abstinence from the permanganate, with restriction to very hot coffee and clam broth for a few days, and the administration of small doses of bismuth subnitrate, restored order and no harm was done. But this is not a safe remedy for casual prescription to patients not under daily observation. Nor is it the remedy for amenorrhea from anemia. The removal of the causes of blood deterioration, the use of iron and arsenic, of calcium lactophosphate, and the roborant regime in its best expression, constitutes the proper line of treatment, resisting the solicitations of the laity who imagine that disaster will surely follow the discontinuance of the flow for a few months.

MENISPERMIN

Standard granule—gr. 1-6, Gm. .01.

Menispermin is a concentration from Menispermum Canadense, or yellow parilla. The plant contains two alkaloids, berberine, and menispermine, or menispine according to Maisch. The latter seems to closely resemble berberine in its action.

Felter and Lloyd say that menispermum is tonic, laxative, alterative and diuretic. From medium doses a slight increase in the volume of the pulse is evident, and the appetite is increased as well as the bowel action. Excessive doses cause purging and vomiting but no other effects. Menispermum is a superior laxative bitter. It is probably of value in leucocythemia, especially when the spleen is affected.

Specific Indications.—Skin brown, tongue coated at base, tip red, irregular appetite, constipation (Scudder).

This plant has had some repute as a remedy for scrofulous affections, but it seems probable that all its virtues may be explained by the presence of berberine, and that that alkaloid will usefully replace the plant.

The dose of menispermin is a grain three to ten times a day.

MENTHOL

Standard granule—gr. 1-12, Gm. .005.

Menthol is a camphoraceous body derived from oil of mint, that in the market coming mainly from a Japanese oil. It is used

externally for many purposes, but little internally. But as it may with propriety replace the old carminatives, it is well that we should be prepared to recognize any effects, physiologic or toxic, coming from this body. Menthol so closely resembles ordinary camphor in its internal effects that the description of either will apply to the other.

Menthol is a local irritant and when swallowed causes a feeling of warmth in the stomach and coldness in the throat and mouth. Large doses cause nausea and vomiting; headache, confusion and excitement with slow pulse and flushed skin. There may be hilarity, delirium, hallucinations, restlessness, or motor excitement passing into convulsions. Periods of quiet alternate which increase until coma is present. Sometimes this occurs without the period of excitement. The spinal cord is depressed and the reflexes sedated by very large doses. The convulsions are due to stimulation of the cerebrum. The heart is slowed somewhat, the vascular tension raised, the capillaries of the skin dilated, the respiration slowed and deepened slightly, normal temperature remains unaffected but fever is lowered.

Menthol possesses considerable antiseptic power, and stops the movement of leucocytes. It is excreted by the kidneys combined with glycuronic acid.

Menthol has proved useful for the vomiting of pregnancy. It may be given for gastric pains, colics and flatulence, in fact for the whole line of affections in which a carminative is indicated.

The dose is gr. 1-12 to 1-4, repeated every five minutes till relief ensues. It is best given dissolved in alcohol, ether or chloroform, and then diffused through a little hot water. The tablets should not be swallowed undissolved, as they may irritate the stomach. Fermentation in the stomach is usually stopped promptly by a small dose—gr. 1-12—of menthol repeated as often as requisite.

MERCURY

Standard granules—Mercury bichloride gr. 1-134, Gm. .0005; mercury biniodide gr. 1-67, Gm. .001; mercury cyanide gr. 1-134, Gm. .0005; mercury protoiodide gr. 1-6, Gm. .01; gr. 1-2, Gm. .03; mercury salicylate gr. 1-12, Gm. .005; mercury with chalk gr. 1-6, Gm. .01; calomel gr. 1-67, Gm. .001; gr. 1-10, Gm. .006; gr. 1-6, Gm. .01; gr. 1-2, Gm. .03; gr. 1, Gm. .06; calomel and capsicum, gr. 2, Gm. .12; calomel and ipecac, gr. 1-8, Gm. .00013; calomel, ipecac and soda gr. 1-10, Gm. .006; calomel and iridin gr. 1-6, Gm. .01; calomel and soda gr. 1, Gm. .06.

Acute mercurial poisoning is usually due to corrosive sublimate. When swallowed it at once causes burning pain in the mouth, throat and stomach; nausea, and vomiting of bloody shreds of membrane; diarrhea, violent tenesmus, dysenteric stools, with

evidences of collapse—small, weak, thready pulse, shallow, rapid respiration, cold, clammy sweat, sunken eyes, the voice sinks to a husky whisper, the face is pinched. There are no constant cerebral symptoms. The face is anxious and denotes the pain from which the patient suffers, which is that of acute gastritis. The urine becomes scanty or stops; the last passed containing casts and albumin, sometimes sugar. Death may occur from shock within an hour, but usually comes later, when the patient has become exhausted by the continued action of the poison. If the poisoning is due to absorption from dressings, corrosion of the mouth is absent but the other symptoms are similar. Salivation and its sequences occur within a few days.

In chronic poisoning the local effects are wanting. It begins with a metallic taste, and soreness of the gums and tongue. One or more teeth feel as if too long, and are tender when bitten upon. The breath becomes fetid, the buccal mucosa swollen and all the glands secrete freely, the tongue is swollen and coated, and ulcers appear along its side and along the edges of the gums. If the ingestion of the poison is continued, these ulcers spread and may become diphtheritic or gangrenous, the teeth loosen and fall out, and necrosis may extend to the maxillary bones. Some rise of temperature is usual. The appetite fails, diarrhea may occur, while erythema, urticaria, eczema, albuminuria, glycosuria, disturbances of menstruation and cachexia, are symptoms observed with more or less frequency. Workers in mercury are liable to erethism, tremor, neuritic pains, anesthesias, affections of the eyes or ears, local palsies, etc.

Physiologic Action.—Taken continuously in doses short of toxic, mercury stimulates all the faculties, physical and mental. All the glandular secretions and excretions are stimulated, the processes of metabolism hurried, the appetite is enormous, the sexual desire and power are increased, and all the bodily and mental functions are stimulated. In fact, the patient feels that he is living at a rapid rate, and using up his vitality fast. The great stimulation of the lymphatics occasions a rapid absorption and excretion of morbid products, and there is a curious feeling of internal "cleanness," a sense of new birth, experienced. With this comes a sense of capacity for great things. This description is based on the experiences of a colleague, who became accidentally inoculated with syphilis, unsuspected until constitutional symptoms appeared. He was then placed on mercury and kept as close to the toxic dose as possible without actually touching it, for a year. When soreness

of a tooth appeared the dose was slightly lowered till the soreness ceased, and after a few days slowly raised again. The theory on which this use of mercury is based is as follows: This drug causes disintegration of the normal tissues when given in toxic doses. The syphilitic tissues which contain the specific cause of the disease, are prone to spontaneous death, and hence are more liable to be destroyed by mercury than the sound tissues. The art of administering mercury then consists in giving such a dose as will destroy syphilitic growths without being strong enough to break down normal cells. For this purpose it is necessary to ascertain what dose will produce the slightest tangible—that is toxic—effects, and keep just below it. The medication should be kept up as long as there is any visible evidence of the malady remaining and for at least three months more; and resumed after this whenever any symptom of the disease appears. By this means, and this alone, the writer believes that syphilis may be radically cured. The treatment should be instituted the moment the diagnosis is satisfactorily made.

Mercury is eliminated through the kidneys, the intestines, and to some extent by all the emunctories. It passes to the mother's milk, and through her blood to the fetus *in utero*. It has been detected in the urine a day after its administration began, and six months after it has been stopped. The form of mercury for use in syphilis is a matter of individual preference, all forms being efficient. The writer prefers the iodides because they are more readily eliminated than other mercurials, and may be combined with other iodides of iron, calcium and arsenic, when desired.

Salivation may be prevented by keeping the teeth in order, with brush and the aid of the dentist, and by using atropine when the danger point has been passed accidentally. Much of the local disease in the mouth is due to the elimination of mercury there, and is easily preventable.

Therapeutics.—Mercury was long used as an antiphlogistic in all fevers and inflammations, but under the attacks of Samuel Thomson and Charles Reade it became unpopular and fell into disuse. It was restricted to serous inflammations, and then to iritis, where it is still employed. We may see a revival of this use any day. The old physicians were a unit in asserting that when the constitutional effects of mercury were manifest the imflammation was obviously undergoing resolution. The dependence of disease upon microorganisms and the superlative powers of mercury as a germicide have given the necessary excuse for a revival of the prac-

tice. Calomel is still employed as a cholagog purgative, and is now generally given in doses of gr. 1-12 to 1-6 every hour till a grain is taken, followed by a saline laxative. It is specially indicated when the stools are white, fetid and acholic. A certain sense of well-being follows mercurial purgation that does not ensue when other purges are employed alone. But the habitual use of calomel in this way is not advisable.

As an intestinal antiseptic calomel is still used in typhoid fever, since Wunderlich showed that the results of other treatment were better when a preliminary dose or two of calomel had been given. Five to ten grains are here advisable. The benefit arises from clearing the bowels of their decomposable contents. In most febrile maladies this is good practice.

As a diuretic calomel was given with squill and digitalis, and possesses unquestionable value. Especially in cardiac dropsies it is of use, to clear the tissues of encumbering fluid while more rational measures, such as the dry diet, are employed to prevent reaccumulation. A grain of calomel, with digitalin gr. 1-67 to 1-22, and scillitin in similar dose, may be given every four hours for four doses.

Especially in opening the treatment of malarial fevers is the calomel purge indicated, followed by salines or purges of the jalapin series.

With children, ill-temper, a muddy complexion and a coated tongue, with indigestion, have been considered indications for calomel, which is always beneficial; but any laxative like rhubarb or juglandin, followed by antiseptics, does the work as well and without the danger.

Mercury bichloride is of value in dysenteries, if given in doses of gr. 1-134 every one to three hours.

Mercury with chalk is an old favorite for children.

The remedy is contraindicated by the cachectic state, general debility, non-syphilitic anemia, feeble digestion, possibly tuberculosis though this is denied, nephritis especially if elimination is defective, and when iodine is being taken or used. Pregnancy is usually a contraindication.

The old superstition that during the administration of calomel, lemonade and other fruit acids may not be given has at last and happily been disproved. Calomel is not transformed into the bichloride in the digestive tract.

Surgeon Wright, of the U. S. Navy, has recently advocated mercurial injections as specific in the treatment of pulmonary

tuberculosis, but his favorable results have not been duplicated by other observers and were probably due to the coexistence of syphilis with tuberculosis.

Dr. N. B. Shade, of Washington, D. C., years ago advocated mercurials by the stomach for tuberculosis, rightly attributing much of the benefit to the intestinal antisepsis.

Poisoning.—In acute mercurial poisoning evacuate the stomach thoroughly. If there is no stomach tube at hand, give the two powders of a seidlitz or soda powder in succession, so as to mix and effervesce in the stomach, which will answer the purpose well and without nausea. Tannic acid or any drug containing it may be given to render the mercury less soluble, and eggs, milk or any albuminous substance to neutralize it.

For chronic poisoning evacuate the stomach and bowels, stop the mercury, use astringent antiseptic mouth washes, with atropine enough to keep the mouth dry, and eliminate by iodiodes given to saturation. At first this will render the mercury in the body soluble and active, and it is not to be given as long as active symptoms of the poison are present. The generally advocated potassium chlorate is inferior to solutions of hydrastine, a grain to the ounce, or of tannic acid, or any of the volatile oils. Careful cleanliness is essential.

MORPHINE

Standard granules—Hydrobromide, gr. 1-67, Gm. .001; hydrochloride, gr. 1-67, Gm. .001; hydrochloride, gr. 1-12, Gm. .005; sulphate, gr. 1-67, Gm. .001; sulphate, gr. 1-12, Gm. .005.

Morphine is derived from opium, the "concrete juice of the Papaver somniferum." It exists in opium in proportions varying from 2.7 percent to 22.8 percent, in combination with many other alkaloids, which also exist in widely differing proportions, and whose effects vary through the whole gamut of action from pure depression to pure stimulation. While the general effects of opium are apt to approximate those of morphine they may prove to be exactly the opposite; and this exceptional condition may appear at a time when life hangs in the balance. For these reasons and others, the medical profession has to a great extent dropped the use of the galenic opiates and employs morphine instead.

Physiologic and Toxic Actions.—All the salts of morphine are insoluble in ether (Ruspini). All are quite soluble in cold water, and in glycerin; which permits the use of the milk sugar granules in extemporaneous watery solution, by the mouth or

hypodermically. The hydrochloride and the hydrobromide are the best salts for ordinary use; the sulphate is good; the acetate is less stable and not so well-defined. As a calmant the hydrobromide should be preferred.

The action of morphine is different as it is given in single or in successive doses. Some persons tolerate it better than others, the idiosyncrasies being inexplicable and truly extraordinary. (Laura.) The abuse or prolonged use of morphine causes grave poisoning, this being pronounced by Claude Bernard the most toxic of the opium alkaloids, death supervening from paralysis of the brain, especially of the medulla and the respiratory center. Toxic phenomena, even tetaniform convulsions, are produced in man, but only by excessive doses, never by well-calculated therapeutic doses. Morphinism is becoming more frequent since the abuse of hypodermic injections, in wasting them, vulgarizing them, even profaning them, and rendering their technic familiar to all.

Morphine causes first a depression of the voluntary movements, later a marked increase in reflex excitability; drowsiness ensues, passing into sleep, that following small doses being rather a state of quiet. The patient may be easily aroused. This state is accompanied in some cases by a sense of well-being, termed euphoria, and this is exceptionally of such delightful quality that the patient once experiencing it craves a repetition. A woman to whom I once gave a hypodermic of morphine told me she felt as if "floating on clouds of bliss." To the majority no such sensations come. The drug is to the intellect a paralyzant from first to last. At first it is the reason and judgment that are paralyzed, self-consciousness is subdued while the fancy is unaffected, so that the patient may shine in conversation and astonish those who only knew him when fettered by timidity or a sense of propriety. With larger doses the coherence of thought becomes confused, the sense of time is weakened but not so markedly as with cannabis, and somnolence comes on as the drug affects the sensorium more. Dreams follow, of pleasant form at first, but later of frightful nature.

Still larger doses cause deep sleep, from which the patient is with the more difficulty aroused as the doses rise. Finally his state becomes that of coma, the respiration sinks in frequency, the pulse is good, the pupils are contracted to a pin point, the face is purple and congested, the skin warm but the axillary temperature below normal, and the nose becomes raw with the rubbing provoked by the itching. The respirations weaken and may assume the Cheyne-Stokes form. Cyanosis creeps in, the pulse becomes faster and

weaker, and the pupils dilate just before death, which is from arrest of respiration, the heart beating feebly after death.

After remedial doses of morphine the patient awakes with headache, dulness, the digestion stopped and appetite lost, the mental faculties sluggish. Delirium and convulsions may occur as idiosyncrasies, or as evidence of defective renal elimination.

The depression of morphine is exerted first on the brain, the stimulation on the cord. Large doses are requisite to produce the latter. Small doses often assuage or remove the pains of disease without destroying consciousness. Sudden shocks are felt when the same injury if gently made will be unnoticed. Small doses have little effect on the motor cerebral centers while large doses lower or abolish their irritability. Cutaneous sensation is lessened. The vascular pressure is raised, the arteries of the skin on the head and neck dilate, and perspiration is increased. As asphyxia advances the pressure varies, though if artificial respiration is kept up this is sustained. The respiratory center is paralyzed before the centers for cardiac inhibition and vasoconstriction are much affected. The peripheral muscles and nerves are only affected by lethal doses. The secretions are lessened, except when nausea occurs, when the saliva and perspiration are increased. The urine is often retained in the bladder.

Morphine checks the movements of the stomach and bowels, as well as the intestinal secretions, and constipates. The excretion of carbonic acid is lessened, lactic acid increases, and glycogen disappears from the liver. Sugar may appear in the urine.

Morphine is excreted mainly in the saliva, gastric juice, intestinal fluids, and a trace by the kidneys. It appears in the stomach two and one-half minutes after injection hypodermically, and ceases to appear there after an hour. Some of it may be oxidized in the body.

Therapeutics.—The place occupied by morphine is peculiar. Like alcohol it does a great many things and does them well; but there are few if any uses to which this drug is put that may not be better accomplished by some one or other of the agents in the hands of the alkalometrist. It is safe to say that morphine will be employed much less frequently, as the physician becomes familiar with the use of definite, uniform agents, and acquires a liking for a certain nicety of applying his therapeutics. Morphine and alcohol are the standbys of the lazy doctor.

The numberless applications in medical practice to which morphine may be usefully put may be classed under four heads; as it

is employed to relieve pain, to induce sleep, to check secretion, and to allay cough, besides some miscellaneous indications.

1. Pain is by no means a simple primary factor, to be treated as such. An aged physician expressed a too common view by exclaiming: "Pain? That means morphine!" Most pains are spasmodic, such as colics, hepatic, renal, etc.; and these are best relieved by remedies that relax the spasmodic contraction of the smooth circular muscular fibers. For this purpose morphine is inferior to the mydriatic group, atropine, hyoscyamine, and especially hyoscine. These potent alkaloids have long been employed with morphine, but few seem to comprehend how little of the efficacy of the combination should be credited to the morphine. Besides, the latter contributes a real and serious peril of its own. Pain antagonizes the action of morphine, so that it has been proposed to combat acute morphine poisoning by inserting a knifeblade beneath the finger-nails, that the atrocious pain may counteract the supervention of fatal coma. In calculous attacks morphine is often administered in rapidly repeated and increasing doses, until the stone rolls out of the duct in which it has been grasped, the pain ceases to antagonize the drug, and the patient dies narcotized. Hyoscine is more effective and less dangerous because it is rapidly eliminated. The conscientious practician will not place too much dependence upon drugs, but if the pain persist after the physiologic action of the analgesic is manifested, will take this as the indication of a fixed mechanical obstacle to the progress of the stone, requiring mechanical means of relief.

A second large group of pains embraces those due to hyperemia of the affected part. Here the circulatory equilibrium may be restored best by the administration of the vascular relaxants, which open up the spastic circulatory areas and allow the blood to flow out of the engorged parts, relieving the pressure on their nerves and the heat of the inflammation. Aconitine and veratrine here afford relief as speedily as and more decidedly than does morphine; they are curative also since they interrupt the progress of the inflammation and prevent the subsequent stages by dissipating the initial engorgement.

A less frequent variety of pain, but one of agonizing nature and perilous in the extreme, is that due to the stoppage of the blood-supply to a part. The writer has not forgotten in a third of a century his vain effort to give enough morphine to quell the pain of an orchitis, strapped so tightly as to stop the circulation. The kind Providence that watches over young doctors and their patients led

him to investigate, find the difficulty, and remove the straps before gangrene had destroyed the testicle. Henceforth he has employed rubber bandages alone for that purpose. Had he here relied on the "morphine for pain" axiom, the result would have been disastrous.

Neuralgia is disappearing from our neurology. The specialists have shown us that persistent and inveterate neuralgias often depend upon material lesions along the course of the affected nerves, requiring mechanical measures for relief. On the other hand, very many neuralgias are undoubtedly explicable by the autotoxemia hypothesis. The blood becomes charged with toxins reabsorbed from the alimentary canal, these act with especial force on the delicate, sensitive nervous tissues, and at the point of lowest resistance an attack of neural pain results. Morphine gives relief by withdrawing the toxins from the blood and throwing them into the cells, where they are stored and inactive; but as the effects of the drug pass off these toxins are thrown out into the blood, reinforced by those constantly being formed in the body metabolism, and the pains recur. Unless evacuants are now given, a second dose of morphine is needed—and thus the foundations of the habit are laid. Such pains are notably relieved by the synthetic analgesics, and these have been of inestimable service in giving immediate relief while the necessary evacuants are doing their work. For the immediate effect of cathartics here is often to increase the pain, by liquefying hard fecal masses and increasing the toxin reabsorption. A weak galvanic current was pronounced by Anstie the most powerful remedy to relieve neuralgic pains, and the writer has many times proved the practical value of the suggestion. When there is reason to conclude that back of an inveterate neuralgia there is degeneration of the roots or centers of the nerves, the phosphide of zinc possesses an efficacy of which few seem to be aware. No other remedy appears to so quickly and markedly improve the nutrition of the degenerated structures and break up the paroxysmal sequence.

One of the uses of morphine most strongly insisted upon is to relieve the pain of injuries, keeping the patient in comparative ease until the surgeon reaches him, and facilitating the latter's work. This applies also to such accidents as the pinching of hernias usually reducible. But while morphine is certainly effective here, it is much inferior to hyoscine as a means of giving relief, and the latter does not increase subsequent suffering by interfering with elimination.

2. As morphine was once the great analgesic, so it was the hypnotic. But who can now suggest a case in which this is the best remedy to induce sleep? Men must sleep, whether they will it or not. The absence of sleep must always mean the presence of some obstacle. The removal of this is obviously the indication—the administration of drugs to cover it up is an unskilful and perilous expedient. Pain is to be relieved by the remedies above mentioned. Insomnia is, barring pain, due to the presence of too much blood in the brain. This may be in turn explained by a lack of vascular tension, with feeble heart-action; the patient is sleepy when erect because the heart has difficulty in lifting the blood to the head against gravity; but on lying down, the cerebral vessels have too weak tension to resist the inrush of blood, and the patient becomes wakeful. This condition is so beautifully relieved by a physiologic dose—that is, just enough—of digitalin, ergotin or strychnine, that it is a pity to overlook such an opportunity of nice, precise medication. But if the cerebral hyperemia be active we have an equally nice and effective remedial application, in a physiologic dose of aconitine or veratrine, or, better yet, of gelseminine.

In the whole realm of insomnias due to mentality—worry, overwork, overexcitement, grief, etc.—the most popular remedy has been the bromides. Their efficacy has been marred by their deleterious effect upon the digestion and their depressing action on the vitality. The new alkaloid solanine affords all the benefits of the bromides, with so little of their disadvantages that they are negligible. If the bromide inhibition of the sexual function be desirable, this may be better accomplished by the use of gelseminine. Bromides will destroy the sexual capacity, leaving desire unaffected; gelseminine checks unruly desire without impairing power. But in all this group of insomnias an elegant, effective and harmless remedy is found in veronal, which seems destined to supplant the entire synthetic group from chloral down. With such remedies for insomnia, we repeat, how can anybody speak of morphine!

3. Morphine certainly checks diarrheal and dysenteric discharges, and some of us have possibly witnessed the death of such patients after opiates had completely stopped the flux. Irritation of the bowels is now so generally looked upon as proof of the presence of an irritant, which is to be gotten rid of, that even in Asiatic cholera there is a constant recurrence of the advice to use laxatives, despite the fully proved fatality of the treatment. Morphine would be effective in all the choleraic group, were it not that atropine is so much more so: The cholera outbreak is an excessive manifesta-

tion of pneumogastric activity, and atropine has no rival as a sedative of the vagus. A hypodermic of this potent alkaloid needs no addition of morphine to control the choleraic symptom-complex, in cholera Asiatica, cholera morbus or cholera infantum. In the latter malady morphine is, next to milk, the most dangerous substance that can be given to the child. The indications are to moderate vagus hyperesthesia, and to empty and disinfect the alimentary canal, rather than to stop the discharges; and even if it be advisable to moderate these, inducing narcotism is not the way to do it. Narcotism is remarkably quick to supervene here, with moderate doses of opiate. Hot enemas, plain, saline, with silver nitrate a grain to eight ounces, or with bismuth subnitrate suspended, are much better remedies in every way, and not at all dangerous.

In no other form of diarrhea is morphine indicated. Mild laxatives, rhubarb, salines, oil, should be employed to clean away irritating substances, and hot enemas to aid this object and soothe the irritation. If astringents are employed, they should be antiseptic, like resorcin, salol or the phenolsulphonates.

In dysenteries, amebic and bacillar, emetine in full doses, hot enemas and quinine flushes, are more effective than any opiate. The only claim recently made for morphine in this group of diarrheal maladies has been that it is needed to check excited peristalsis. Here morphine is not as effective as atropine, however, and the temptation to hurry matters and secure present ease by a narcotic dose is apt to be too strong for the patient or nurse. Many deaths have been the result.

Laura advises morphine in nervous erethism, hyperesthesias, and neuropathies in general, for the dolorific and spasmodic elements. But this was before the introduction of gelseminine, cicutine and solanine, which relieve these morbid conditions as effectively and promptly as does morphine, and without the peril of a drug habit, almost inevitable in such patients. The writer has for many years made it a rule never to allow to any neurotic a dose of any opiate whatsoever.

4. To relieve cough: First be sure you want to relieve the cough. If there is secretion, it must be ejected. If dry and tough, or scanty, emetine, apomorphine, lobeline, and the inhalation of steam, offer an ample stock of useful remedies. To allay excessive irritation we have zinc cyanide, cannabis, and if any opiate is needed it should be codeine, a better remedy for this purpose than morphine. For the whole group of nervous coughs hyoscyamine is more effective than morphine or any other opiate.

5. In lead colic, if, as Laura suggests, we employ hyoscyamine and strychnine, we have a remedial combination whose efficacy is not enhanced by the addition of morphine. Nobody who is familiar with the values of gelseminine would think of employing morphine for the insomnia, restlessness or other nervous symptoms attending febrile disease. In asthma the relief from morphine is uncertain, temporary at best, and if it is at all satisfactory the formation of the morphine habit is assured. Morphine certainly gives temporary relief in cerebral anemia and in affections due to that condition. It does not remove the anemia and is more than likely to aggravate the underlying cause. If this symptom requires direct medication, we have a more powerful and less objectionable remedy in atropine.

The time has long passed when any opiate was employed in the treatment of alcoholism. Looking on this malady as a toxemia, the elimination treatment has supplanted the narcotics completely. No hypnotic will induce sleep in these cases so surely as will emetine, and the effect of the latter on the course of the disease is remarkable. The same may be said of the delirium of fevers; elimination, support, nutrition and circulation regulators leave no place for morphine. It is unnecessary to give the very objectionable opiates for afterpains, when a grain or two of caulophyllin, or a little gelseminine, will quell them effectually. Few will be inclined to give morphine in albuminuria, despite the weighty authority of Huchard. Should a calmant be imperatively required it should be an eliminant like veratrine or gelseminine; or, if cerebral anemia be marked, glonoin and hyoscyamine.

Possibly the strongest case for morphine may be found in the control it sometimes exerts over glycosuria. Here there is a curious *lapsus* in our knowledge: Experiment has shown that neither morphine nor codeine is as effective as crude opium. Obviously, some other of the twenty-six or more activities entering into the chemistry of opium excels the two alkaloids named; but no experiments have ever been recorded to show which of the others is the remedy. At the best, opium is only a palliative, and of questionable utility in the long run. The curative treatment of diabetes is fairly successful. Diabetic toxemias are perilous and the effect of morphine on the digestion is disastrous.

When the physician was confined to the older forms of crude vegetable preparations, there was some reason for the general use of morphine. Since the genius of Merck has placed in our hands a long list of active principles, whose effects in health and in dis-

ease have been ascertained by the precise experimentation only possible with such remedies, we are enabled to apply our therapeutics in the treatment of disease with a precision impossible a generation ago. The art of fitting remedies to the aberrations from normal function presented clinically, is one that is well worthy of our most careful study. There is far more to clinical therapeutics than the careless prescription of half a dozen drugs to every case, with a little "jollying," and the employment of a trained nurse. My plea is for a more careful study of pathologic conditions as presented during life, and greater care in the application of remedies. In no other department of our art do such rich rewards await the investigator.

Norris says that where eclampsia occurs in a woman who has nephritis previous to becoming pregnant, morphine is a dangerous drug.

Morphine is the remedy for emergencies, to relieve by hypodermic when there is great pain and other remedies are not at hand. Apart from this the field for the legitimate use of morphine is exceedingly restricted. In diabetes it certainly checks the output of sugar, but we have been unable to find any case cured by it.

Dr. C. L. Lackey, of Missouri, was called to see a woman in the fourteenth convulsion of puerperal eclampsia, antepartum. He injected half a grain of morphine sulphate in each arm and the patient promptly went to sleep. In about one hour she awakened and had another milder spasm. A half grain of morphine was injected in one arm. After an hour and ten minutes she had another seizure and another half grain was administered. In a few minutes the respirations indicated for the first time that she was getting the full effect of the drug. At about the same time her pain increased in frequency and force, with the os only slightly dilated. In about three hours dilation was sufficient to permit application of the forceps; an eight-pound boy, strong and healthy, was delivered, with very little evidence of the heroic dosing of the mother. During this instrumental interference the woman slept peacefully, being completely insensible to pain; and she continued to sleep for eight hours. At the end of that time she gradually regained consciousness, called for food and drink and from that time on had an uneventful convalescence. Since that time he has treated nineteen cases similarly, without loss of either mother or child.

Poisoning.—The treatment of acute opiate poisoning consists in emptying the stomach promptly, and sustaining the respiration.

Hypodermics of strychnine are useful, with artificial respiration. As long as this is sufficient it is worse than useless to try to prevent sleep. Large doses of coffee combat the effects of the drug to some extent, but atropine enhances some morphine effects while combating others. The inhalation of oxygen is a useful measure.

MYRICIN

Standard granule—gr. 1-6, Gm. 0.01.

Myrica in regular medicine—which does not use it—is simply an astringent, acting through its tannin content. The eclectics, who speak from actual clinical observation, have more to say of it. The Thompsonians used it in gastrointestinal catarrhs. Others have used it with success for scrofula, jaundice, diarrhea, dysentery, aphthæ and other diseases where astringents are desirable.

Lloyd says that in small doses it stimulates the vegetative system of nerves, aiding digestion, blood making and nutrition.

In larger doses it is a decided gastric stimulant. Chronic gastritis, chronic catarrhal diarrhea, mucoenteritis and dysentery with typhoid character, respond to small doses. It is said to restore arrested lochial discharges. Cases calling for myrica show feeble venous action, the pulse full and oppressed. Locke advised it in scarlatina with swollen, enfeebled tissues, as antiseptic and stimulant. Fahnestock employed myrtle wax in epidemic dysentery with typhoid symptoms: it is mildly astringent and narcotic.

Specific Indications.—Profuse mucous flows; gastrointestinal catarrhs; atonic diarrhea, typhoid dysentery, atony of the cutaneous circulation, full oppressed pulse.

The study of vegetable active principles has not yet progressed sufficiently for us to intelligently select from the numerous forms of tannic acid that one which most accurately fills any one of the pathologic conditions requiring astringents.

NARCEINE

Standard granule—gr. 1-67, Gm. .001.

Narceine is an alkaloid from opium. It is found in an average proportion of 0.2 per cent. Many years ago Da Costa published an account of some trials of narceine in the Reports of the Pennsylvania Hospital; in which he concluded that this agent had little if any value. But the narceine then furnished was probably too impure to warrant any deductions whatever from its trial. The same may be said of the specimens from which Claude Bernard derived

his very favorable opinion of this alkaloid. We must have recourse to modern observations made with agents of undoubted purity before advocating or condemning a drug.

Narceine is soluble in 945 parts of alcohol at 80 per cent, easily in boiling alcohol, not at all in ether, benzole or petroleum ether, slightly in chloroform and in amylic alcohol. It has little affinity for acids, but forms crystallizable salts with hydrochloric, sulphuric and nitric acids.

Physiologic Action.—Van Renterghem experimented with pure narceine. He took evening doses of gr. 1 1-2, followed by slumber calm and more profound than usual; waking with a sense of heaviness in the root of the nose and the forehead, remaining till afternoon; the narceine did not interfere with the customary morning dose of saline laxative, but the stools were less liquid. The appetite was unaffected, and there was no dryness of the mouth or coating of the tongue. One day, when he was suffering with slight diarrhea and abdominal pains, an evening dose of narceine, gr. 1 1-2, induced sleep and calmed the intestinal disorder. Next day there were no abnormal sensations, the bowels acting as usual. A young woman of 20 suffered with a cough "ferine," and he gave narceine and iodoform a granule each, every quarter-hour. Next day the cough had ceased. She had emptied two tubes of 20 granules each and now took them every hour.

To a woman of 26 affected with uterine epithelioma and suffering the atrocious pains that prevented sleep, resisting galenic opiates, Rabuteau gave a vaginal injection containing narceine. One hour later the pain had disappeared, the patient was soundly asleep, and on his next visit she thanked the doctor warmly. This happy result was repeated. He also obtained satisfactory results from narceine in sciatica, neuralgic pains of various sorts, relieving and even curing them with narceine, which often proved superior to morphine. As a remedy for cough this alkaloid was praised by Laborde in whooping-cough, by Line in acute bronchitis, by Oettinger and Levis in asthma.

As a muscular relaxant it has succeeded in hysteric convulsions and spasmodic contracture of the limb that had resisted morphine (Eulenberg).

Rabuteau says: "This precious substance also arrests diarrhea. Not only does the intestinal mucosa secrete less under its influence, but the buccal, pituitary and even the conjunctival mucosa show a sort of desiccation. Thirst augments as with morphine. Often doses of gr. 1 1-2 to 3 are required to obtain these results, and diar-

rhea is not as well arrested as by morphine. Narceine is nevertheless to be preferred as not causing nausea or anorexia, especially with phthisical cases where narceine relieves these disagreements."

Exceptionally writers have mentioned as due to narceine, vertigo, ringing of the ears, headache, nausea and vomiting on waking, or excitement and insomnia.

Hypnotic doses, after a period of acceleration of the pulse, slow the heart and the respirations; if the narcotic stage is prolonged there may even be a lowering of the temperature (Eulenberg, Sichtung).

The pupils do not contract during the sleep of narceine, and the reflex excitability is less dulled than after morphine (Sichtung).

Fabini and Ottolengui state that narceine increases the excretion of urea. Its prolonged use induces tolerance.

Laborde finds narceine perfectly tolerated by infants.

Injected under the skin it diminishes tactile sensibility as morphine does; introduced into the eye it does not affect the pupil (Eulenberg).

Narceine is eliminated chiefly through the urine and the bile (Dragendorff and Schmemann).

Therapeutics.—Van Renterghem recommends narceine as a succedaneum for morphine in treating women and children, weakly persons and those unduly susceptible to opiates. Narceine is useful when it is important to avoid the constipation of morphine. As a hypnotic narceine does better for persons bedfast, gravely ill, than for the well; it is specially valuable in insomnia caused by obstinate cough, as in phthisis. Valledor values it above codeine as a remedy for coughs.

Burggraeve also advised narceine for harsh, painful coughs, and as a calmant of the nervous system. It is an anodyne analgesic in the pains of inflammation, if given in suitable doses even during the height of the fever, associated with the other modifiers demanded by the case. It is then rare that this remedy does not lessen the pain, spasm, agitation and fever. In neuralgias, headache, intercostal neuralgia, gastralgia and sciatica, narceine often succeeds when morphine fails. Here aconitine, gelseminine, butyl-chloral, atropine or cicutine should be associated as indicated.

The granules of gr. 1-134 each, Van Renterghem gives to a newborn infant without division, every hour if necessary. Older children can take two to five granules at each dose. It may be given hypodermically. Harley's formula is preferred: Pure narceine 3 parts, glycerin 45; warm slightly to perfect solution, then add

1 part hydrochloric acid and 2 parts distilled water. This makes a solution of one part to twenty—or 5 percent.

Narceine has received little attention at the hands of American alkalometrists, because the tendency here is to make little use of opiates, and when unavoidable to substitute codeine for morphine. But the foregoing account of the French investigations show that there are values in narceine that should not be overlooked.

Proposition—that narceine excels morphine in pain-relieving power, as compared with its effect in abolishing consciousness.

NARCOTINE

Standard granule—gr. j, Gm. 0.06.

Narcotine forms about 6 percent of opium, the percentage varying widely.

The formula is $C_{22}H_{23}NO_7$. It resembles codeine somewhat more closely than it does morphine, but has less depressant action than either. In frogs it causes some depression, quickly followed by an increase of reflex excitability like that produced by strychnine. In mammals the depression is still slighter, followed by excitement, restlessness, tremors, increase of reflex excitability even to convulsions, ending in death; the symptoms exactly coinciding with those of strychnine. The pulse is slowed by direct action on the heart. Very large doses have been taken with little or no narcotic effect, narcotine being much less toxic than codeine (Cushny).

Narcotine is considered a cotarnine opianate. Narcotine is obtained by exhausting opium with water, treating with hydrochloric acid, precipitating with sodium carbonate, and crystallizing in alcohol in the presence of a little animal black. It forms handsome needle crystals, insoluble in water, soluble in hot alcohol, in chloroform, and in 33 parts of ether (Bocquillon).

Narcotine possesses antiperiodic properties similar to those of quinine, which it is said to excel. It causes diaphoresis. It is the least toxic of the opium alkaloids (Claude Bernard), less convulsant than thebaine and papaverine, while doses of 0.40 Gram (gr. 6) do not induce somnolence.

This agent has been used in India for malarial affections, in doses of Gram 0.05—0.15 (Shaughnessy), and narcotine sulphate in doses of one Gram (Root).

When narcotine is oxidized, oxygen and water are abstracted and the base is decomposed into opianic acid and cotarnine. The hydrochlorate of cotarnine has been termed stypticin, from its

styptic properties. The formula is $C_2H_4NO_4Cl$ (Merck gives it as $C_{12}H_{13}NO_3HO\ HCl$). It is a yellow crystalline powder, very bitter, easily soluble in water and in warm alcohol. The solutions are yellow, but become darker on exposure to light. Its chemical constitution closely approximates that of hydrastinine, differing by the substitution of the methoxyl group, OCH_3 for an atom of hydrogen. The physiologic effects confirm this close relationship. In frogs stypticin causes central paralysis. In mammals large doses cause narcotism, followed by paralysis, death occurring from paralysis of the respiratory center. The fatal result can be prevented by artificial respiration. No influence on the circulation could be detected, wherein it differs from hydrastinine. Nevertheless, clinical observation has demonstrated that stypticin possesses valuable hemostatic properties. This is especially the case with uterine hemorrhages. It is useless in hemorrhage from uterine cancer. So also, it has proved ineffective in hemorrhages depending upon pelvic exudations and ovarian congestions. In menorrhagia and metrorrhagia it has proved exceedingly effective. The drug is well tolerated by the stomach. Pregnancy does not contraindicate its use (Liebreich), as it does not cause uterine contractions.

Rousse and Walton pronounced stypticin a tonic to the circulation, especially the heart, and useful in hemoptysis. The dose is Gram 0.20 (gr. 3), best given hypodermically in the gluteal region (Gottschalk). In very severe menorrhagias he gave it four hours before the expected flow. By the mouth, Gram 0.025 (gr. 1-2) five times a day, in capsule or tablet; the latter being preferable on account of the bitterness. Hypodermically it may be injected in 10 per cent watery solution (Merck).

It has proved especially effective in the profuse menstruation of young girls, and in those occurring about the climacteric. Merck recommends it in doses from gr. 3-4 to 4, five times a day.

Gottschalk gives stypticin the preference over other hemostatics in dysmenorrheic hemorrhages, on account of its sedative, anodyne and soporific properties. In subinvolution the hemostatic effects were in every case permanent, which would indicate the valuable power of contracting the connective fibers, but not the muscular tissue of the enlarged uterus. The action is primarily on the nervous centers, lowering the rapidity of the respiration and secondarily the blood-pressure. It is therefore a relaxant hemostatic, for active hemorrhages.

Boldt has found stypticin useful in acne, rosacea, eczema, urticaria, etc., when connected with menstruation. Munk found it

effective in restraining hemorrhages following the extraction of a tooth, by inserting a tablet in the cavity. He suggests the same local application for the bleeding following circumcision. It is not, however, a local blood-coagulant, but a true hemostatic, acting by vasoconstriction of the small vessels.

Bloch recommends stypticin topically for parenchymatous bleeding from cavities.

Marcus found its internal use ineffective in checking bleeding occurring in dental cases, but the direct application never failed, besides being painless. Hulisch testifies to the efficacy of stypticin applied locally, in dental work upon notorious hemophiliacs. Munk found 10 percent solutions strikingly successful in checking epistaxis, and Jahl succeeded in the same cases by applying stypticin gauze.

Among the authorities who have reported favorably on the hemostatic property of stypticin are Boldt, McGee, Gottschalk, Nassauer, Gærtig, Bakofen, von Braitenberg, Bossi, Freund, Nedorodow, Pazzi, Paoletti, Zaramella, Heyden, Abegg, Walther, Lavialle, Ruyssen, Munk, Bloch, Jahl, Marcus and Hulisch.

NICKEL BROMIDE

Standard granule—gr. 1-6, Gm. .01.

Nickel bromide is a deliquescent salt, of greenish color. It was introduced to afford the benefits of the bromides in a small dose. In therapeutic effect gr. 1 1-2 equals half a dram of potassium bromide.

Da Costa employed nickel bromide in epilepsy with success. Hare recommends it in melancholy and hysteria.

In large doses Cushny ranks nickel with cobalt as a poison.

Like the other bromides this sedates the functions of the brain, dulls the sensibility of the faucial mucosa, and allays irritability of the sensory nerves. It sedates the sexual function without destroying desire, rendering erection impossible. A like influence is exerted on the ovaries. The reflexes are sedated, the motor power diminished and the vascular tension relaxed. The heart is slowed and weakened, but not as much as by potassium bromide. Very large doses slow the respiration and lower the temperature. Cerebral anemia is produced, according to Hammond. As a mild and harmless sedative the bromide of potassium has been employed to an enormous extent of late; and yet beyond a limited field there is no evidence of its usefulness. Tons of this drug have been ad-

ministered as placeboes, or with very little idea of its effects beyond a temporary masking of symptoms by lowering sensibility.

Therapeutics.—Cerebral fulness and irritability in children are relieved by a few small doses of bromide; but as these usually come from some irritating substances in the alimentary canal, the old practice of administering a dose of ipecac or of castor oil, though less pleasant, is indubitably more efficacious and rational.

In the grave cerebral and meningeal imflammations we have never witnessed any benefit from the enormous doses of bromide usually given. Purging and vascular sedatives are immeasurably more effective; especially if followed by absorbents. In exophthalmic goiter veratrine is better; with cicutine hydrobromide. When goiter coincides with irritation of the genital apparatus the bromides will give temporary relief. But there are few more objectionable practices in modern medicine than drugging down the sensibility by bromides. Much better find the causes of irritation and remove them. And it cannot be without harm that a drug which so markedly depresses the sexual power, that index of the vital force, is given so freely and continuously as this. The practice of medicine teaches the lesson of using every possible means of increasing and cultivating the vital forces; and the use of depressants, unless temporarily, is a bad tendency.

In epilepsy the bromides have long been relied upon by the profession, to such an extent that the routine consists in giving enough to ward off the paroxysms, neglecting every means of ascertaining and removing the causes of the malady. Sometimes it requires huge doses to do this—the writer has given to an epileptic an ounce of potassium bromide a day for seventeen months. But it is better to give nickel bromide up to 10 grains a day, then if the fits continue add arsenic bromide to strengthen the bromide effect and prevent acne, adding successively the other small-dose bromides, of gold, mercury, cicutine, etc., till the fits cease. Meanwhile the sources of morbid irritability are to be found and removed and the morbid impressibility of the nervous system allayed by appropriate treatment moral, and especially hygienic. There is no easy or general method for the treatment of epilepsy.

When it is desirable to reduce the sexual ardor, the bromides may be given freely; though gelseminine, salicin, and the sulphides, accomplish this object at least as well.

The authors do not approve of long-continued bromidizing. The dose of nickel bromide for an adult is one to five grains, and this may be pushed up to 15 grains a day.

NUCLEIN

Standard tablets—gtt. 1-2, and gtt. 2. Nuclein Solution.

Nuclein can be and often is obtained from the egg, the spleen, the thyroid gland and other portions of the animal economy, but as a matter of uniformity and to avoid danger from decomposition it has been found better to procure it from live cereal germs, involving, however, chemical processes which require much time and labor.

Physiologic Action.—When administered hypodermically, nuclein promptly produces a rapid increase in the number and activity of the leucocytes. This increase varies somewhat with the subject and the disease from which he suffers, but in all cases there is a most decided augmentation. The polynuclear cells are particularly affected. These cells, as has been shown by Metchnikoff, are the most active of the phagocytes. That the bactericidal power of the blood serum when free from corpuscular elements is due to nuclein is now believed; this nuclein is found free in the blood and is supposed to be secreted by the leucocytes. The administration of nuclein has been shown to increase this bactericidal power of the blood many fold. The effect of a dose passes away in from thirty to forty-eight hours, hence the necessity of continuous administration. Care, however, should be exercised not to overwork and thereby exhaust the cells. In some cases the exhibition of large doses at longer intervals is better than the continuous use of smaller quantities.

Briefly, the whole practical basis of nuclein therapy is the increase of leucocytosis. By its administration we obtain an increase in the phagocytic action and furthermore add to the number of these natural defenders of the body's health. When the system becomes so depleted by disease and the presence of morbid germs that cell repair is hindered or stopped altogether, we are face to face with a condition that has baffled science throughout the history of intelligent medication. Now the discovery of nuclein enables us to so stimulate cell-formation and phagocytosis that the *materies morbi* is surrounded, consumed and thrown out of the body as waste while at the same time the normal restoration goes on.

Therapeutics.—In all cases of infection of the system as well as in all anemic and chlorotic conditions nuclein will prove valuable. If given *per os* it is necessary to give it on an empty stomach and to give no water so as to secure quick absorption from the buccal mucous membrane and the stomach. In phthisis its administration is followed by a prompt fall in the temperature

and a general amelioration of all symptoms. Indolent ulcers take on a new aspect, and, as granulation progresses normally and rapidly, are soon healed. In typhoid fever and other diseases where marked deficiency of leucocytic action is evident it is an excellent adjunct to all modes of treatment, and the worst of these will produce better results with nuclein than the best without it. In malarial dyscrasias, in intestinal and gastric difficulties and in fact in all forms of disturbed metabolism (and therefore faulty cell repair), this agent should be used freely. The list if carried out would thus embrace all conditions of lowered vitality, the acute infections, such as diphtheria, tonsillitis, typhus and all the exanthemata, most disorders of the liver and nearly all the diseases of the skin.

When administered in doses of two to ten drops of the medicinal solution nuclein soon causes a feeling of stimulation and well-being, and many a time improvement has been manifest from the very first dose.

In the following list of diseases to which nuclein is applicable, we present a few hints that we trust will be helpful and incite to fresh study.

Anemia.—Here the dose of nuclein must be reasonably small. It has been demonstrated that if administered in five-to ten-drop doses, two or even three times a day, there is a rapid increase in the red blood corpuscles, but if larger doses are taken and oftener and continued for some time, there is almost as rapid a decrease.

It should be remembered that anemics are as a rule always constipated.

Arthritis calls for nuclein, more especially in those patients who have become anemic through prolonged uric-acid poisoning. Salicylic acid may be used locally with advantage and the emunctories should be kept open.

Asthma per se cannot be controlled by nuclein, but its exhibition gives the patient a better systemic condition and thus enables him to throw off the disease more easily under appropriate treatment. This consists to a great extent of elimination and cerebrospinal tonics. The attacks are controlled usually with glonoin, or apomorphine, strychnine, hyoscyamine and glonoin one granule of each dissolved in a little hot water and given every ten or fifteen minutes. Iodized calcium should not be forgotten; in fact, it is clearly indicated in most cases.

Bronchitis in all its forms responds quickly to nuclein medication. The prompt use of iodized calcium with tonic treatment is suggested as abortive.

Bronchopneumonia.—The dose of nuclein should be large, ten to twenty drops given hypodermically every four or six hours. Give strychnine and arterial sedatives in the early stage. When there is capillary involvement the use of potassium bichromate is followed by prompt improvement. Emetine and brucine are the drugs that prove most efficacious in children's cases.

Cancer.—Nuclein has brought about a marked improvement in many instances, and when combined with condurangin locally, it is perhaps one of the most reliable remedies that we possess. Full dosage—preferably hypodermically—for a prolonged period, and in the periphery of the growth, gives best results. Half an ounce of the standard solution, injected hypodermically, three times a week, has afforded the best results. This is four times the dose at which leucocytosis ceases to rise and the division or destruction of the leucocytes begins. The action that is curative of cancer seems to be that which destroys the leucocytes.

Cholera infantum in its early stages is controlled beautifully by small doses of atropine, copper arsenite and nuclein. The latter is best given here in solution which can be dropped on the child's tongue.

Chorea.—In this disease the most beneficial results have followed full doses of nuclein given for a prolonged period, the Triple Arsenates with Nuclein being usually a good form.

Debility, general and senile, naturally calls for nuclein, but it must be given more as an adjunct to strong and prolonged tonic treatment; the use of nutritious, easily-digested and sometimes predigested food should, if nuclein, strychnine and arsenic are exhibited, soon cause any weakness to vanish.

Diabetes mellitus has been influenced most favorably by nuclein. If the proper diet is ordered and arsenic and gold bromide are exhibited, together with hypodermic injections of increasing doses of nuclein every day a fair percentage of cases will go on to cure. A. J. Weaver, of Iowa, reports rapid relief and apparent cure of diabetic gangrene of the foot, in a man aged 70, by the use of nuclein solution in doses of 15 minims four times a day, with tincture of iron.

Diarrhea, when it assumes a chronic type, leaves the system in just that condition which calls most imperatively for nuclein. Its administration should be begun early and with it strychnine, hydrastine and the Intestinal Antiseptics (W-A) should be given. Small doses of a saline laxative are often called for, but its use must be determined by the type of case. The acute form needs

small doses of calomel followed by a saline and after the bowel is thoroughly emptied, the intestinal antiseptics.

Diphtheria.—In this dread destroyer of the little ones the doctor who does not use nuclein, peroxide of hydrogen and calcium sulphide is open to defeat. Here as in other diseases it is important to have an exaggerated leucocytosis present, and as already pointed out the larger the dose of nuclein the more rapidly can this condition be produced. The solution should be injected promptly in fifteen or even thirty-drop doses repeating every six or eight hours for the first two or three days; after that it is safe to continue the medication *per os*. Peroxide of hydrogen must be used freely and usually pure, the fauces and nasal passages being flushed with it every quarter hour. Calcium sulphide should be given to saturation, and iodized calcium should be exhibited in five-grain doses t. i. d. The heart needs sustaining with strychnine and cactin, the former being replaced in the case of very young children by brucine. Elimination must be kept up. Antitoxin of course.

Dysmenorrhea cannot naturally be influenced directly by this remedy, but the patient will be benefited generally and the doctor will have better material to work upon if nuclein and the tonic arsenates are exhibited. Here, too, watch and see that elimination is kept up.

Eczema and nearly all skin disorders are the outward manifestation of a general bodily dyscrasia and nuclein will prove of great benefit. There are but few forms of skin disease—if indeed there be any—which will not yield sooner or later to thorough and continuous elimination, blood building and an aseptic bowel.

Exanthemata.—In all the eruptive diseases the administration of nuclein is of great benefit. It makes no difference how the case is treated otherwise, the addition of nuclein *per os* or hypodermically will prove of benefit. The one point that needs attention is the dosage. The small dose, *per os*, in the early stages once or twice daily, and in latter stages of a severe or badly-treated case full doses hypodermically give best results. Calcium sulphide, tonics and always elimination are also indicated.

Exophthalmos is another disease which in its early stages yields with marked rapidity to nuclein hypodermically. In these cases there is always a defective metabolism together with more or less nervous irritation.

Fever.—The best treatment is to administer one of the arterial sedatives, aconitine, gelseminine or veratrine, in small, frequently-repeated doses, support the heart with digitalin or strychnine and,

at the same time, aid elimination. Given in moderate dose nuclein promotes oxidation, favors the elimination of waste and all deleterious products and, finally, and most important of all, stimulates the phagocytes and enables these soldiers of the system to surround and destroy the invader.

Influenza (la grippe) is again but an evidence of cell disturbance and retention of toxins. Clinical experience has demonstrated that the theory that here nuclein should be the remedy is correct. After compelling free elimination see to it that the heart is supported with strychnine, etc., and the body rendered an unfertile and uncongenial field for the influenza bacillus by saturating the patient with iodized calcium, and finally, with nuclein, aid in the restoration of normal cell function.

Leprosy.—Yusuf, of Turkey, reports the cure of a characteristic case of leprosy by injections of nuclein solution, continued for five months.

Pharyngitis (Follicular) is readily controlled by nuclein through its action on the body secretions, but with it should be given calcium sulphide to saturation (especially in the beginning) and hourly doses of potassium bichromate, gr. 1-67.

Phthisis.—It would be really repetition to point out the indications for the use of nuclein in phthisis. Be the general treatment what it may, there is only one remedy which can possibly restore cell-activity and that is nuclein. The dose should be carefully gauged; five drops every day will do at first but this should be gradually increased as necessity may arise. The best effects have been obtained from daily hypodermic exhibitions. Ward's use of nuclein here seems destined to mark an epoch.

Rheumatism.—The main effort should be to get rid of the toxic matter in the system at the time and prevent, by improving the general *tonus*, the manufacture of more. Calcalith, colchicine and salines are *the* agents *par excellence* with which to "clean out" and, after this has been done, then nuclein is the remedy with which the patients' condition may be rendered somewhat more nearly normal.

Tonsillitis and quinsy have been cured so quickly by the use of nuclein that its specific character in these diseases is generally allowed. As soon as the first symptoms appear, begin to administer small doses of calomel (say 1-6 grain every half-hour for eight doses), follow with a laxative and throughout give every two hours ten drops of nuclein solution. After twenty-four hours the acute condition will as a rule subside, then the nuclein should be continued

for a week, three times a day. Apply the full strength standard solution to the affected area.

Septicemia.—In septicemia nuclein gives the most brilliant results. Wherever it is possible to get at and remove the source of the trouble the administration of nuclein, with calcium sulphide and elimination, enables the system to rally and dispose of the poisons which have already gained access to the circulation.

Struma.—Strumous and rachitic children, generally intractable cases, will improve rapidly on nuclein and calcium salts with skin friction, exercise and proper diet. See that the alimentary canal is emptied and that the digestive processes are in good order.

Syphilis.—In syphilis, nuclein and stillingin should be given to full effect together with mercury protoiodide; beginning with the latter in small doses and gradually increasing the dose to full tolerance.

Typhoid Fever.—While this is to be treated generally as directed under the head of "Fevers," there are a few things to be remembered which apply here particularly. When nuclein is given in full dosage, along with intestinal antisepsis and free elimination, there is established, as has already been pointed out, an artificial leucocytosis, with the result that in a few hours the entire character of the disease is changed for the better.

In the treatment of intestinal perforations in typhoid fever. Chantemesse recommends hypodermic injections of sodium nucleinate to increase hyperleucocytosis and the vital resistance of the patient.

During *pregnancy* the use of nuclein is strongly indicated and in the few cases where it has been used the results, both as regards mother and child, have been quite remarkable.

The aged benefit very much by full doses of nuclein given three times a day together with saline laxatives in the morning and two to three granules of the Trinity at bedtime. Nuclein is reconstructive, fortifying the body against rapid waste, hence the above indication.

In children of a dwarfish habit, or those who seem to be delicate without apparent cause, we are almost certain to find defective assimilation, both primary and secondary. Nuclein, with proper eliminative remedies, is indicated.

Administration.—Hypodermic Injection. In giving nuclein hypodermically it is imperatively necessary that not only the syringe and needle be sterile but that the skin itself be surgically clean. The most satisfactory plan to follow is this. Use only a

solid metal or glass syringe. The whole syringe should either be soaked in alcohol or boiled for a few moments. While this is being done the skin over the site of puncture should be washed with ethereal soap or plain soap and water and then sponged off with alcohol or ether. Now with a five-percent solution of carbolic acid go over the spot again and finally dry with sterile, absorbent cotton. Cover the area with a wad of this while getting ready to inject.

Having wiped off the syringe with cotton (sterile), draw up the amount of nuclein you propose to inject from the bottle direct and if for constitutional effect add at least an equal quantity of distilled water, but if for local action—as in cancer, etc.—inject pure.

See that the fluid is well up to the point of the needle before injecting and after ejecting a drop wipe off the needle with cotton soaked in alcohol and with a firm hand push it well home under the skin. Inject the nuclein slowly, withdraw the needle and seal the puncture with a touch of collodion.

If these measures are taken you will never have the chill or flushing which some practicians claim to follow the injection of nuclein. This simply means that some septic matter was injected with the nuclein and as some of the preparations are from animal matter it is easy to see how a mild septicemia can follow the use, without aseptic precautions, of such a nuclein solution.

Dose of Nuclein by Mouth.—There is something in the manner of exhibition. When a rapid and marked leucocytosis is desired the dose should be ten, fifteen or twenty drops and repeated every three or four hours. If, however, the general tonic and sustaining effect of nuclein is desired the dose should be small, five drops being the maximum—and this should be given not oftener than three times or better twice a day. One thing has been proved by experience and this is that nuclein should not be taken within an hour of eating. The best time is when the stomach is most nearly empty, as absorption is more rapid and complete and there is not the probability of chemical change taking place. When the digestive function is active there is an undoubted loss of effect. It is well to hold the nuclein in the mouth to be absorbed thence directly.

PAPAYOTIN

Standard granules—gr. 1-67, Gm. .001; gr. 1-6, Gm. .01.

From the pawpaw, Carica papaya, is derived an enzyme, papayotin, which has the power of digesting all the elements of a

meal, fat, starches and albumin. It forms peptone. It acts at any temperature, and in either acid, alkaline or neutral conditions, though it acts more quickly in alkaline solutions. It has no action on the body when taken into the stomach, simply digesting the food and nothing more. Its powers as a universal digestant of all forms of food render it widely applicable. It has been proposed to utilize it to digest intestinal parasites, but this seems doubtful. It has been injected into tumors, where it forms peptones, but the utility of the procedure has not been proved. Solutions will dissolve the membrane of croup and diphtheria, but the malady is not affected. Injected into the blood it paralyzes the heart and nerve centers, and causes intestinal hemorrhages. Injected in watery solutions of any strength into the subcutaneous tissues it causes great pain and inflammation, with high fever.

Finkler credits papayotin with antiseptic powers, and Shoemaker says it can be given with salol or weak solutions of corrosive sublimate. Dr. E. A. Wood praised it as an application in ozena, tuberculosis of the larynx and lungs, etc. It has been urged as a galactagog, and to dissolve cerumen from the ear. Sittmann reports its value in diarrheas due to indigestion, and acute gastritis. It has proved useful in dilatation of the stomach.

The dose of papayotin is a grain before or with the beginning of each meal. As with the other artificial digestants, the benefit is less in the quantity of food digested by it than in starting up the digestive process. The great value of papayotin lies in its power to aid in indigestions of all forms, whether of fats, starches or albuminoids. Add to this that it is not so liable to decomposition as the animal products like pepsin, and it acts irrespective of its surroundings, whether acid or alkaline.

PELLETIERINE

Average dose—0.5 Gm.—7 1-2 grains.

To the labors of Tanret we owe our ability to replace the nauseating decoction of atrocious taste and uncertain strength, by the alkaloid of small dose, no irritation, of little taste, and of constant strength. The savant chemist discovered in the pomegranate bark four alkaloids, volatile and liquid, with one exception, and forming crystallizable salts with acids.

Pelletierine is soluble in alcohol, ether, chloroform, and in twenty parts of water. Isopelletierine differs only in its polarity. Pseudo and methylpelletierine are much less toxic to parasites.

Pelletierine exerts upon the human body a pronounced action. Beranger-Feraud observed vertigo after small doses; after four to six decigrams (grains six to ten) by the stomach, vertigo, troubled vision, heaviness of the eyelids, often diplopia, cramps of the arms, tremors of the fingers and toes, frequently nausea and vomiting. Rochemure noted after hypodermic injections of gr. 2-3, heaviness of the head; after gr. 1 1-2, vertigo, weakness and disturbed vision; while gr. 8 determined the same symptoms, but more accentuated.

The toxic effects are manifested after six to eight minutes, if given hypodermically; after one-half to one hour when given by the stomach. Once after a dose of gr. 8 by the mouth Huesemann-Hilger noted general muscular paresis, worse in the lower extremities, so intense that the patient had to lie down.

Von Schroeder concluded that pelletierine increases the reflex excitability of the cord up to tetanic accesses, with slight cerebral paralysis at first; the muscles are affected as by veratrine, but not so strongly; the peripheric terminations of the pneumogastric are paralyzed. These conclusions resulted from observations on the frog. On warm-blooded animals he found this agent caused excitation and increase of the reflex irritability; marked disorder of the locomotor function; transient stimulation of the vasomotor center and increase of vascular tension; and pneumogastric paralysis.

Some persons compare the sensations after full doses to drunkenness; the senses are clear but the legs fail to do their duty. The toxic symptoms last two or three hours and subside slowly.

The dose required to cause expulsion of the parasite is about six grains. Brute found two tenia expelled by this dose, but next day the patient was affected with choleraic symptoms.

Von Schroeder enumerates among the qualities of a good anthelmintic that it should be toxic to the parasite and not dangerous to its host; and that it should not be absorbed from the stomach, but penetrate to the intestine to act against tenia. Pelletierine is not very toxic to man.

As tenia from man were not obtainable, experiments were made with the tenia serrata of the cat. This was found to live for many days when immersed in Bunge's saline solution. When pelletierine was added in the proportion of one to 10,000 the worm became motionless in five minutes, but could be revived by changing to a fresh saline solution. But when exposed to the drug for ten minutes it could not be revived.

Pelletierine sulphate does not fulfill von Schroeder's conditions, as it is quite soluble in water, and readily absorbed from the

stomach. But in eighty-eight cases in which pelletierine was administered with an equal dose of tannic acid, to delay its absorption, the entire worm was expelled in eighty-two cases.

The socalled tannate of pelletierine is rather a mechanical mixture (of one part of the base to three of the acid) than a chemical combination. As the tannin is responsible for the gastric and intestinal irritation caused by this dose, it would be wiser to give the sulphate, in keratin coating, if that substance really does what Unna declared—passes its contents through the acid stomach to be delivered undiluted and unabsorbed in the alkaline bowel. Moreover, as it requires about five to six grains of pelletierine to kill the worm, it will take double that quantity of the tannate; and as both are costly, and quoted at the same price, it costs twice as much if the tannate is prescribed.

Van Renterghem advises a single massive dose to be taken, alone or with tannic acid, followed in half an hour by any effective purgative. The administration of an equal quantity of the alkaloid in fractional doses throughout the twenty-four hours is far from exerting the same effect.

The pelletierine of the shops is often composed of all four alkaloids of pomegranate, and should be given in double the dose advised for the pure drug. Of the tannate the dose should be from ten to twenty grains.

The dried bark is inert. The greatest proportion of pelletierine is found in the bark of the stems, that of the root containing mainly the weaker methypelletierine. The bark should be collected before flowering, as there is then the largest quantity of the active principles. The strength of barks from different countries varies widely. In France that from Portugal is preferred. From Java comes probably the best. Those who prefer the galenic preparations are thus favored with an extensive supply of uncertainty as to the real value of the stuff they inflict on their confiding patients.

PEPSIN

Standard granule—gr. 1-6, Gm. .01.

The pepsin of the shops is obtained from the stomach of the pig. It acts only in the presence of hydrochloric acid, the best results being obtained from solutions containing 0.2 percent of acid. It digests only proteids. In very many cases where pepsin has received credit it has been due to the acid alone. There is often a deficiency of acid when pepsin is secreted in abundance. Cushny

therefore limits the use of pepsin to cases where proteids are not digested even when enough acid is present. Pepsin wines are believed to be inert, but it requires a stronger alcoholic solution to destroy its proteolytic power. The presence of superfluous peptones in the stomach at the end of digestion prevents the action of pepsin. Alkalies are incompatible with pepsin; mercury, lead, zinc and copper prevent the action of pepsin by precipitating it. Tannic and gallic acids, creosote and phosphorus are also incompatible. Strong alcoholic fluids interfere with its action. Pepsin digests pancreatin and other digestants.

In addition to its uses in indigestion of albumen, pepsin has a certain therapeutic power peculiar to itself. It has long been known that preparations containing it are effective in allaying irritation of the stomach, the vomiting of pregnancy, sea-sickness, etc.

The average dose of pepsin for an adult is a grain at the end of each meal, with a due addition of hydrochloric acid.

PHYSOSTIGMINE

Standard granules—Physostigmine salicylate, gr. 1-1000, Gm. .0000625; gr. 1-250, Gm. .00025.

Physostigmine is an alkaloid derived from the Physostigma venenosum, the ordeal bean of Calabar. The plant contains at least two other alkaloids, calabarine which resembles strychnine, and eserdine which acts like physostigmine but is milder.

It is also called eserine. It is of a very complex composition, and its salts are easily decomposed in a watery solution, developing a red color. It is an intense poison.

Physiologic Action.—Physostigmine resembles pilocarpine in action. It depresses the nerve centers, and kills by paralyzing the respiratory center. Consciousness is intact after the respiration is gravely affected and the muscular force weakened. Some preliminary stimulation is probably induced. Muscular twitching occurs, and the irritability and power of the muscles are increased by moderate doses. The respiration is at first faster, then becomes slow and weak. Small doses slow the pulse and raise vascular tension, larger ones slow the heart still more and the pressure falls. The action on the heart is direct, not through inhibition. It produces powerful contractions of the stomach and intestine, and increases all the secretions—tears, saliva, perspiration, mucus and pancreatic juice. It causes contractions of the bladder, ureter, uterus and bronchial muscular structures. It contracts the pupil but accommodates the eye for near vision.

Harnack holds that physostigmine acts on the secretory gland cells and on the muscular fibers; but others believe that it acts on the nerve-ends in these structures.

Its effect extends first to the many organs that are provided with smooth and striated muscular fibers, and also to certain glandular organs, all of which this poison generally irritates. Formerly it was thought that the irritation affected the muscular fibers themselves, but at present there is an inclination to regard the irritation of the poison as affecting the terminal distribution of the nerve-fibers to the muscles and glands. It is not definitely settled whether the beautiful crystals of physostigmine salicylate of the pharmacopeias are identical with the original physostigmine that was obtainable only in an amorphous combination.

Physostigmine is eliminated mainly through the kidneys, appearing a few minutes after ingestion. Traces appear in the saliva and the bile.

Van Renterghem took during a day about gr. 1-22 of Merck's pure crystallized physostigmine. He experienced a peculiar sensation in the throat, as of a morsel that could not be forced down except by repeated strong efforts. This began five minutes after each dose and reached its maximum of intensity in half an hour, disappearing within three-fourths of an hour. As this effect was uniformly experienced he attributed it to local action. No other effect was noted but a slight diminution of the appetite. Next day he took about gr. 1-20, in divided doses, gr. 1-100 every hour. By noon he felt slight vertigo; with little appetite. Little by little the malaise augmented; in the stomach he felt a sense of spasmodic non-painful movement; no nausea; firm stool with discharge of urine; more vertigo, face pale, whole body cool without shivering, nails blue, sweat on forehead and over face; fatigue; easier when half lying down. At 12:30 energetic intestinal peristalsis, stool, followed by three vomitings, not preceded by nausea. No bile thrown up. Slight desire to sleep; no more vertigo but felt cold; pulse normal at 76 to 82; now 64; axillary temperature 36.8 C. No ocular symptom. By 2:30 all had subsided, heat returned, temperature 37.1, pulse 70. At 3 p. m., resumed taking physostigmine gr. 1-300 hourly till 10 p. m. Dined at 5, little appetite, frequent urination, no other effect. At the hour of retiring the pulse was 76, temperature 37.4 C. A good night.

Therapeutics.—As a depressor of the cerebrum it has been used in epilepsy but under its use the paroxysms increase in frequency and violence. In chorea the same result has been recorded.

It has failed also in tetanus. In flatulence it is one of the most efficient remedies at our disposal, and has never failed the writer. In cases of chronic morphinism when the cheek shows a dusky flush, the capillaries passively dilated, the brain probably in a state of passive dilatation of its capillaries, physostigmine in doses of gr. 1-100 hypodermically gives exactly the sensations of morphine, and the patient is unable to detect the difference. This has rendered this agent useful in the treatment of such cases. The dose must not be repeated more than once in twelve hours, or increased, or the depressing effects of the drug become manifest and it does harm.

M. E. Douglass says that physostigmine increases the contractility of the muscles of the bladder walls and of the uterus. It is a motor depressant in large doses, while in small medicinal doses it has a contrary influence. He advises it for the hypertension induced by extreme nervous irritation, and finds that convulsive disorders from irritation are allayed by it. He says that in medicinal doses it stimulates the respiratory function and heart action, where there is great depression with difficult breathing and a sense of compression or constriction of the chest, with soft, feeble pulse, cool, moist skin, and usually dilated pupils. It is the remedy for dyspnea under such circumstances. It is also advantageous when the dyspnea is caused by clogging of the bronchi and air-cells, without power to expel the thick, tenacious mucus. Here it liquefies secretion and increases the power to expel it.

In emphysema and in asthma with great muscular relaxation, also in bronchitis with dilatation, he finds it useful. It restores tone in phthisis and overcomes night sweats. He thinks it might prove advantageous in dilatation of the stomach, in atony and extreme inactivity of the intestinal muscular structure. In intestinal catarrh from this cause it is of much service. It is also of value in catarrh of the mucous linings of the kidneys and bladder, and in extreme atony, relaxation and plethora of the abdominal structures. He finds, however, its chief field in diseases of the eye. When mydriasis has been induced by atropine, physostigmine quickly restores the normal condition. Adhesion of the iris occurring from inflammation may be broken up by it. It is used to reduce intraocular tension, to increase the power of accommodation, in conjunctival inflammations where perforating ulcer threatens to permit prolapse of the iris, when ulceration without determination of blood is present, intermittent strabismus, glaucoma, asthenopia, photophobia and sometimes in neuralgia of the eyeball. After

injury to the eyeball many conditions may occur which will be promptly relieved by this agent.

Physostigmine has been utilized by ophthalmologists to contract the pupil, to oppose the effects of atropine, and in treating glaucoma.

Dr. J. C. Dreher details two successful cases of tetanus. The first was treated by physostigmine in doses of 1-4 grain hypodermically. This was repeated every hour for four hours, by which time all the symptoms had ceased, and there was perfect relaxation of the muscles, a copious bowel movement and free action of the kidneys. Rapid recovery. This was in the case of a boy of thirteen.

The second case was that of a boy of nine years. The alkaloid physostigmine not being at hand, an effort was made to substitute the fluid extract of physostigma; thirty drops of this was injected every hour. Next day there was but little if any change. The dosage of the injections was increased to sixty drops, and in another day the improvement was marked.

A third case described by the same writer was treated on so-called modern principles at a hospital. The patient died after the third injection of antitetanic serum.

In connection with the above the writer will say that he has frequently noted that after maximum injections of physostigmine, such as 1-50 of a grain, very marked depression ensues, such as will follow very large doses, such as 1-3 of a grain, of pilocarpine. It is only in very small doses that physostigmine exerts a stimulating action; in large doses it is sedative and relaxant. These cases are notable. The treatment should be especially commended to the attention of those who have used physostigmine in tetanus, giving 1-100 of a grain, stopping at that and not pushing the remedy to the dosage employed so successfully by Dr. Dreher.

Van Renterghem cites many cases in which tetanus was cured by physostigmine, even tetanus neonatorum. It is not a remedy for strychnine poisoning. Animals fed with both die sooner than when strychnine alone has been administered. Subbotin found it useful in fecal impaction, and with belladonna and nux it has become a common prescription for constipation. Maschka cured a case of diarrhea with flatulence, due to intestinal catarrh, by the use of physostigmine.

Harnack says that the effects of physostigmine, especially that prominent stimulating effect which it has upon the heart-muscle, would make it excellently available for medicinal purposes

were it not that it has at the same time an exceedingly violent effect upon the central nervous system which is eminently perilous to life. For this reason the remedy is at present limited almost wholly to external use, while formerly the unreliable extractive preparation from the bean was used internally, as for instance in tetanus neonatorum.

This remedy is of great value for the eye specialist as a myotic which by repeated instillations contracts the pupil even when moderately under the dilating influence of atropine. It is also useful in tearing up posterior synechia, also to prevent prolapse of the iris or to reduce it when prolapsed, which may happen in operations on the eye. The most important service of physostigmine is in glaucoma, for its power of contracting dilated blood-vessels can be used in that disease to reduce the internal pressure of the eyeball by contracting its dilated blood-vessels and thus save the eye in many instances.

Physostigmine salicylate consists of colorless or yellowish, glistening, small crystals which are soluble in water, the solution becoming reddish after some hours and losing in efficacy, hence must not be kept too long. It is used for instillation into the eyes. (1 : 500 up to 200 parts of water.) Maximal internal dose is from one to three milligrams (0.001 to 0.003), and for children from 1-40 to 1-20 of a milligram (0.00025 to 0.0005).

Physostigmine sulphate is more soluble in water, not distinctly crystallized, and is used mostly in veterinary practice.

Physostigmine Poisoning.—Since the use of the remedy became more limited to external applications the poisoning accidents with it are rarely met with now, either in medical practice or otherwise. Yet caution should be observed in its external use as well, for absorption is not excluded. A few milligrams in an adult, and half a milligram in a child, can have bad consequences. The first toxic phenomena, apart from pupillary contraction from local application, consist in an increase of secretions, vomiting, diarrhea, intestinal spasm, colic, tenesmus, cardiac palpitation, slowed pulse, then also violent muscular twitchings, spasms, psychic excitement, dyspnea, etc., and finally paralysis of respiration.

The treatment, apart from the exhibition of evacuants, has to be directed to artificial respiration or oxygen inhalation. As an antidote atropine hypodermically and in not too small doses is recommended, which however cannot be designated as a perfect antidote to physostigmine. Muscular cramp can be stopped with curare, but the danger is in impairing the breathing.

Poisoning by Calabar bean is treated by evacuating the stomach, giving atropine enough to antidote the toxic effects, and employing supporting measures. Atropine antidotes physostigmine more effectually than physostigmine does atropine.

Van Renterghem recommends to begin with doses of gr. 1-250 to 1-134 of physostigmine salicylate or sulphate.

The daily dose of physostigmine should not exceed gr. 1-50, divided, for an adult.

PHYTOLACCIN

Standard granule—gr. 1-6, Gm. .01.

Phytolaccin is a concentration from Phytolacca decandra, or poke.

The chemistry of this plant is obscure, a number of active principles having been assigned it, but none of them has been placed on the market or shown to represent the virtues of the plant. Our most voluminous information concerning it comes from the eclectics.

Felter and Lloyd say that phytolacca acts upon the skin and the glands, especially those of the mouth, throat and sexual apparatus, and most markedly on the breast. It also acts on the fibrous and serous tissues and the digestive and urinary mucosa. It is eliminated mostly by the kidneys. It slows the heart and reduces its force, as well as that of the respiration. It paralyzes the cord, acting principally on the medulla. Tetanic convulsions are produced by toxic doses. Death results from paralysis of respiration. In full remedial doses it acts as an emetic and drastic cathartic, the vomiting being preceded by an hour of suffering. The subsequent purging lasts long. Large doses cause violent emeto-catharsis with muscular paralysis, occasionally spasms, and frequently tingling or prickling. Dimness of vision, diplopia, vertigo and drowsiness are caused by large non-fatal doses.

Therapeutics.—Phytolacca is emetic, cathartic, narcotic and alterative, and has been advised for dyscrasias, scrofula, syphilis, chronic rheumatism; it relieves osteocopic pains better than opiates; destroys the itch acarus; is called for in indolent states of the skin with vitiated blood, chronic eczema, syphilides, psoriasis, tinea capitis, scaly, vesicular, pustular or tuberculous eruptions, varicose and other leg ulcers; with iridin in sycosis, fissures, fistulas, boils, carbuncles, dermal abscesses, and ulcerations at the outlets of the body; tracheitis, laryngitis, influenza, catarrh, especially with diphtheritic tendency; tonsillitis, follicular pharyngitis, stoma-

titis, aphthae, nursing and ordinary sore mouth, and syphilitic faucial ulcers; non-malignant diphtheria; chronic tonsillar hypertrophy; goiter, ozena and nasal catarrh; pharyngeal coughs; the best remedy for hard lymphatic enlargements; acute mastitis, parotitis, metastatic mumps, orchitis, sore nipples, the tenderness of the breasts that occurs during menstruation, ovaritis, lymphoma, subinvolution, uterine and vaginal leucorrhea, felons; gastric and intestinal glandular ulcers; gonorrhea and nocturnal irritability of the bladder; conjunctivitis, gonorrheal, syphilitic and simple; piles; hydrophobia; angina pectoris; many headaches; asthenic hyperemia of spleen, liver or uterus; albuminuria; with iridin in abdominal tuberculosis; obesity; fatty heart if rheumatic; locally for cancer and ulcers.

Specific Indications.—Pale mucosa with ulcers; sore mouth with small blisters on tongue and buccal mucosa; white sore lips, epidermis separating; hard sore enlarged glands; mastitis, orchitis, parotitis, aphthae; sore breasts with impaired breathing; faucial, tonsillar or pharyngeal ulcer; pale sore throat with cough or respiratory disease; white glaze over mouth, in children; white pultaceous sloughs at mouth corners or in the cheek, and diphtheritic deposits.

In case of poisoning by this plant, the treatment consists in emptying the stomach, and keeping up the respiration by hypodermics of strychnine.

Ellingwood advises phytolacca in the angina of scarlet fever, abdominal pains increased by pressure, rectal ails, gastric headaches, the irritation from teething, and in pains in the liver with enlargement and induration so that the patient cannot lie on the right side; in spasmodic and membranous croup, and in neuralgias.

The great repute in which phytolacca is held was originally based on its remarkable action in mastitis. Many times the writer has applied to the inflamed breast of the parturient woman the extract of this plant, with excellent effect. But as it acts through absorption it is better to give it internally, in small and frequent doses. Give gr. 1-6 to j repeated every half-hour till slight nausea begins to be felt, and then less frequently. Support is better than any remedial drug locally. Do not let the nurse rub the breast.

As a remedy for obesity phytolacca should be given daily for three months. No effect may be manifest until the end of this period, when the fat suddenly begins to subside so rapidly as to send the patient flying to her physician. This ceases when the drug is discontinued.

PICRIC ACID

Assuredly, picric acid must have friends, for it continually bobs up as a remedy for something, and will not stay buried. Generally it is as a remedy for malaria internally, or for burns externally. Let us see what there is to be said of it.

Picric acid, trinitrophenol, $C_6H_3(NO_2)_3$, is obtained by treating phenol with nitric acid. It is slightly soluble in cold, more freely in hot water. It is very bitter. It imparts a yellow color to the tissues, urine, skin and eyes, which is removable (when locally applied) by alcohol, boric acid, or strong soap.

Erb credits it with causing nausea, vomiting, diarrhea, emaciation, and strongly affecting the red blood cells.

King says overdoses cause extravasations of blood under the intestinal mucosa, with flatulence, depression and twitching of the muscles.

Ellingwood adds to the list of toxic effects lowering of temperature and blood pressure, respiration becoming shallow, the heart weak and rapid, painful diarrhea and collapse. Sometimes convulsions precede death. The leucocytes are increased in number.

Therapeutics.—Picric acid has been frequently recommended for malaria; reports as to its efficacy vary. King limits its use to cases where quinine has failed or ceased to be beneficial. He speaks of it as a tonic-astringent, useful in convalescence from acute fevers, in headaches, chronic diarrheas, gastric irritability from dyspepsia, anemias, etc. Ammonium picrate is preferable to the acid, as the latter is apt to cause cramps. In malarial debility it has proved useful, also in bilious diarrheas, and as a sedative to spasmodic coughs, either whooping-cough or persistent dry hacking with dry tongue and throat (Ellingwood).

Webster recommends picric acid in pernicious anemias and leukemia, giving very small doses.

Clark found this agent useful in malarial neuralgias, but that it was liable to cause urticaria. The yellow tint of shoe-linings is due to picric acid, and this has given rise to painful dermatitis, with vesication.

Shoemaker speaks of the application of a 6-percent solution for erysipelas. A saturated watery solution—about 1-2 percent—has been often applied to burns of the first and second degree, on compresses. As it dries, the same solution should be employed to moisten the dressings before removal, to avoid injury. It is also applied in ointment of 1 to 2 percent.

Quinquaud applied this acid in epithelioma; while Calvelli advised it in chronic eczema, in solution of 1 1-2 parts in 250 of distilled water.

It should not be applied to extensive burns, as it will cause toxic effects by absorption.

King gives the dose of picric acid or its salts as gr. 1-2 to 1, three times a day. Ellingwood gives that of ammonium picrate as gr. 1-8 to 1-2, while Shoemaker puts it at gr. 1-2 five times daily.

The acid has failed as a remedy for trichina and intestinal worms, and Adler tried it as a surgical dressing and condemned it.

The important point in all this is the use of this remedy in cases of malaria that have resisted quinine, and where the latter has lost its good effect. When a new remedy is tried in such conditions and proved beneficial, it is sure to be lauded as superior to the ones formerly used; when in point of fact it may only be of use in the exceptional cases, or when the worst of the attack is past. Thus the iodides acquired an undeserved repute in rheumatism, where they are only of value in the subacute stages; and copaiba forms the basis of cough remedies that succeed "when all others fail," because that brings the case along to the stage at which copaiba is of use, and if given too soon it can only do harm.

The picrate of iron may be used in doses similar to those of the ammonium salt, when the anemia indicates that metal.

PICROTOXIN

Standard granule—gr. 1-134, Gm. .0005.

Picrotoxin is a glucoside from Cocculus Indicus or fish berries. It has some relations with the digitalin group, for they slightly stimulate the areas around the medulla, while the picrotoxin group do the same thing more powerfully, though they do not affect the heart and vessels as digitalin does.

Picrotoxin may cause vomiting, or salivation, fast pulse and respiration, or slow pulse and palpitation. Stupor and unconsciousness follow and then strong convulsions, tonic and then clonic, affecting the limbs and jaws. There is an arrest of breathing during the spasms, which alternate with periods of quiet. If death occurs it is from asphyxia.

The action is exerted mainly on the medulla, the cerebrum and cord being unaffected. The heart is slowed by stimulation of inhibition mainly, in part by direct action on the heart. The marked rise in vascular tension is also due to centric stimulation.

The acceleration of respiration is likewise due to centric stimulation. Near death the breathing may become slow and labored. When given in doses too small to cause convulsions picrotoxin lowers the temperature.

Picrotoxin is antidoted by chloroform and chloral; and when the respiration is weakened by chloral, picrotoxin restores it, raises the blood pressure, and cuts the sleep short. It may possibly antidote morphine.

Fish berries are so called because they are employed to catch fish. The powdered berries are mixed with bread and dropped in the water; fish swallowing the dose are temporarily stupefied and float on the surface of the water. Consciousness is soon restored and the flesh does not become toxic to the eater of the fish. A tincture of cocculus is used to destroy lice. Death has occurred from this application. Cocculus is also employed as an adulterant of beer.

Tschudi says picrotoxin causes alternating clonic and tonic spasms, killing in 1 1-2 hours; slight narcotic action on the brain, frequent vomiting, and increases the secretion of saliva and bile remarkably. Strychnine causes only tonic spasms, kills in three minutes; does not act on the brain, cause vomiting or affect the secretion of saliva or bile.

Picrotoxin causes drowsiness, stupor, coma, and sometimes delirium. If the dose is too small to produce death quickly, the prominent symptoms are headache, vertigo, nausea, general depression, mild anesthesia, incoordination, and spasmodic muscular twitching. Large doses depress the heart, even stopping it, the pulse later becoming faster (Cushny). Perspiration increases, also the secretion from the mucous membrane of the mouth, thorax, trachea, and bronchi.

Murrell says picrotoxin raises temperature; Cushny says it lowers temperature when the dose is below the convulsant point. Burt says it causes ovariouterine hyperesthesia and spasmodic pains, with general muscular prostration.

Picrotoxin is eliminated by the kidneys and skin. Strychnine and pilocarpine are antagonistic to some extent.

Atropine, chloral, and diffusible stimulants are antagonistic.

Picrotoxin has been used with success for the night-sweats of phthisis. Cushny attributes this action to increased respiration, preventing perspiration through asphyxia. French thinks the best results are obtained by combining picrotoxin Gram .001, agaricin Gram .005, atropine Gram .0005, to be taken together at bedtime.

One writer reports its use as a remedy for nasal catarrh, with perfect satisfaction, the dose being half a milligram, three to ten times a day.

G. Patterson employs picrotoxin as a routine measure to prevent the vomiting following chloroform or chloroform-ether anesthesia. Small doses were injected hypodermically as soon as the anesthetic was withdrawn.

Therapeutics.—Picrotoxin has been recommended as a tonic in dyspepsia, with torpid intestinal walls; it relieves flatulence and colic; for gastralgia, nausea, dizziness and other symptoms of poor digestion. It has been used with success in epilepsy, chorea, alcoholic tremor, shaking palsy, migraine, dysmenorrhea, etc. Anemic nocturnal epilepsy is especially benefited by this remedy. Profuse sweating sequent to influenza was checked by it (Semmola). Murrell recommends it in the night-sweats of phthisis in doses of gr. 1-67 at bedtime or three times a day. It succeeds when even atropine fails.

The most obvious use of picrotoxin would be as a respiratory stimulant but this appears to have been neglected. As a substitute for pilocarpine it would be of use in many instances, the dose being smaller and the price much less.

The dose of picrotoxin is gr. 1-67 three times a day, or half this much every two hours till effect.

PILOCARPINE

Standard granule—gr. 1-67, Gm. .001.

Pilocarpine is a liquid alkaloid derived from Pilocarpus microphyllus, or jaborandi. This exists in the plant in combination with at least three other alkaloids, jaborine, jaboridine and pilocarpidine. Of these one possesses in a lesser degree the qualities of pilocarpine and the others oppose this action through its whole range. The relative proportions and actual quantity of these vary in the plant under the various conditions under which it grows, and which group prevails is a matter to be determined by experiment. It was a case of this that first led the writer to the study and use of the alkaloids. Attending a woman in confinement, she had too little milk for her babe, although fully strong enough to afford it a full supply. The fluid extract of jaborandi was given her to increase the flow of milk, but next day she had none at all. The physician charged the druggist with having made a mistake, the druggist passed the charge along to the manufacturer, and

he to his employees. At that time the chemistry of the plant had not been studied sufficiently to show wherein the trouble lay.

Physiologic Action.—In medicinal doses pilocarpine causes within fifteen minutes flushing of the skin, and either salivation or sweating. Weakly persons, such as victims of organic heart disease with failing compensation, are more apt to have salivation; the more robust the patient the more likely he is to sweat. The sweating from a full dose is very profuse indeed. The discharge contains an increased quantity of the solid constituents of the perspiration as well as the water. It includes urea also. The vascular pressure falls and the temperature if above normal falls from 1 to 4 degrees. Reichert found that the production and the dissipation of heat were at first increased and later decreased by pilocarpine. Nearly if not all the secreting glands are similarly affected. The gastric and pancreatic secretions are largely increased, the bile less so, the tears, milk and bronchial mucus augmented—so much so that full doses have been followed by pulmonary edema.

The discharge of urea by the kidneys is increased, but the water is lessened by the loss through other channels. If given in doses too small to cause sweating, however, pilocarpine increases the urinary flow. It contracts the uterus so strongly that abortion may result. It reduces the size of the enlarged spleen. Children are less susceptible than adults and more apt to show the salivary effect, especially if less than four years of age (Demme).

Remy tells of one case in which a series of epileptic attacks followed the use of this agent. Sudden death ensued in another case.

The writer once gave jaborandi to a puerperal woman to increase the production of milk. She was a very large, portly woman, strong as a horse, but accustomed to the daily use of beer in moderation. In this instance the jaborandi increased the secretion of milk satisfactorily, but in a few days the patient requested the physician to have her confined in an asylum for the insane as she could not much longer resist the impulse to kill her husband with an axe. The jaborandi was discontinued and the homicidal impulse subsided. The milk also ceased entirely, as had been the case at each previous accouchement.

This case was published, and some years later a Russian journal published a report from a physician in Siberia, detailing a similar case, and quoting that recorded by the writer. Yet this does not appear to be a direct action of the drug, but for some unknown reason this woman could not supply her children with milk, and if

any other means had been employed that would have induced a secretion of milk the same mental condition would probably have supervened.

Van Renterghem says that pilocarpine excites the peripheric terminations of the pneumogastric. (The statement in Shoemaker that it paralyzes this nerve must be a misprint.) He truly places the beginning of its notable action at three minutes from the time it is injected subcutaneously. Cerebral tension is felt, with throbbing arteries. The sweating ceases within one hour, the salivation continues longer. If the patient is covered up in bed the sweating may last several hours. Some shivering may follow.

Robin found the average flow of saliva after pilocarpine to be 500 c. c. The sweat ejected is from 300 c. c. upwards—very far upward sometimes. During the action there may be thirst, anorexia, nausea, vomiting (rarely, and more apt to occur if the patient has eaten shortly before taking the pilocarpine, or if he swallows the saliva), slight colic or diarrhea. The desire to micturate becomes imperious, even painful. Thirst, anorexia, dryness of the skin and throat, fatigue and depression, persist some time after the sweating has ceased. At first the pulse gains 10 to 20 beats, subsiding towards the end of the sweating; the rhythm may be disturbed, if the heart is not sound. Arterial tension is but little lowered by strictly therapeutic doses. The pupil is contracted by the local application of pilocarpine. The intraocular tension is lessened. Not only is the intestinal glandular secretion increased but peristalsis is stimulated (Albertoni). The effect on the uterus is greatest at the end of pregnancy (Lavrand).

Six grains of pilocarpine were dispensed by mistake and taken in a single dose by an adult. The symptoms were enormous, but had subsided in four hours. The effects of this agent are attributed to a stimulation of the termini of the excito-secretory nerves; the substance intermediary between them and the gland cells (Vulpian).

Caustic alkalies, per salts of iron, and metallic salts in general, are chemically incompatible with pilocarpine. Atropine is markedly antagonistic. Muscarine, nicotine, apomorphine, physostigmine and picrotoxin, are to a greater or less extent analogous in their action with pilocarpine.

Goyon and Kareff state that pilocarpine lessens and suppresses the glycogen of the liver. When given in full doses it increases the urine and pancreatic secretion, but not the cellular elements of the latter. The increased activity has been explained as due to the increased presence of leucocytes in the secretion. Pilocarpine

injected intravenously decreases the glycogen of the liver, and increases the glucose in arterial blood.

Pilocarpine is being adulterated with sulfonal; as both are soluble in alcohol, this is not detected when pilocarpine is used in hair washes. The sulfonal is not soluble in water, and the adulteration was detected by a physician who was trying to make a hypodermic solution of pilocarpine.

Pringle employed pilocarpine nitrate, 1-6 grain injected into the scalp hypodermically for anesthesia. In one week there was a growth of downy hair over the scalp. The dose was increased to 1-3 grain, with satisfactory results.

Therapeutics.—As a diaphoretic no known drug equals pilocarpine. In all acute pulmonary affections, due to catching cold, a full dose of pilocarpine will often break up the attack if taken in time. In acute exacerbations of chronic respiratory affections, bronchitis, laryngitis, the debut of pneumonia, pleurisy, this medication is well placed. When the sputum is scanty and tough pilocarpine aids by inciting a freer secretion. In dropsies, whenever diaphoresis is admissible it is the most effective agent at our command. In nephritic cases it is equally available when uremia threatens, since it eliminates urea through the skin.

In the dropsy following scarlet fever pilocarpine has proved excellent. Cardiac dropsy does not come under its rule—weak hearts contraindicate it. In many skin diseases pilocarpine has been employed with varying results. As a remedy for itching it has no superior. The itching of jaundice is completely relieved except that due to cancer of the liver. The substitutive action of pilocarpine is often of value here, and the aid given the eliminants renders it useful in all cutaneous maladies traceable to the effort of the skin to supplement the action of kidneys unequal to their task. By this means we may obtain temporary relief and time to institute the methods that tend to cure by equalizing the tasks with the capacity.

E. W. Saunders pronounces pilocarpine the first of eliminants, and almost a specific in many of the infectious diseases associated with faucial and buccal symptoms, such as measles, scarlet fever, the first day of diphtheria, influenza and tonsillitis. He also uses it in erysipelas. For inflammation of deeper tissues he prefers veratrum. He attributes the value of pilocarpine to eliminating toxins, washing away bacteria and stimulating leucocytosis. He gives it until salivation is evident and sustains this for twelve to forty-eight hours. He insists that it should be given early. It

will not have a full physiologic effect in presence of high temperature. This must first be reduced. Pilocarpine sometimes produces vomiting; unless excessive this need not matter as it may be needed. In cases of weak heart or embarrassed respiration, pilocarpine is dangerous and should be avoided. He sometimes combines calomel with it as a glandular stimulant.

The eruptive and other essential fevers may afford a field for this drug as yet unsurveyed. The writer has employed pilocarpine for twenty years as a specific for sthenic erysipelas without finding a case it failed to control. The first case was a stout Irish woman with facial erysipelas, bright red eruption, high fever, some delirium. Pilocarpine was given until slight action was noticeable, by which time the eruption had begun to pale and recede. When it had been reduced to an inch the medicine was suspended, and at once the erysipelas began to spread. Again and again the drug was given till nearly well, and suspended till the redness was evidently spreading, until we were completely satisfied that pilocarpine controlled that disease as we control a trotter with the lines. Then the medicine was given till the eruption had completely disappeared. This experience was repeated with every succeeding case of erysipelas for years, till we met a case of asthenic form, eruption pale, no fever, heart weak from fatty degeneration, the whole system depressed. No tendency to sweating was manifest under pilocarpine, which depressed the strength still more. This patient responded at once and strongly to dram doses of tincture of chloride of iron given every four hours. Since then the writer has met no case of erysipelas that did not quickly respond to pilocarpine if sthenic, and to iron if asthenic.

Dumas reports the use of pilocarpine in 65 cases of yellow fever, without a death. The cases where the drug proved most serviceable were where the urine was scanty and loaded with albumin, the skin hot and dry and the patient comatose. If the pulse was very uncertain he reinforced the pilocarpine with strychnine gr. 1-40. If the effects of the first dose were inefficient, he repeated it.

We must emphasize the use of pilocarpine in the beginning of acute pleurisies. Empty the bowels freely and fully, give a full dose of pilocarpine, enough to cause profuse sweating, and forbid all food and drink. The blood vessels will be drained of serum, the surplus will flow out of the hyperemic capillaries, and the attack be jugulated. The same applies to all acute affections due to catching cold. The abstinence is essential.

Pilocarpine has been employed in several ocular maladies, subacute and chronic; as a myotic it is unequal to eserine; as promotive of absorption it is indicated in iridochoroiditis, and iritis serosa, glaucoma, detachment of the retina, etc.

Schuller reported some cases in which pilocarpine had strongly stimulated the growth of the hair, curing alopecia and restoring gray hair to its original color. Success and failure have been reported as to this suggestion, and as yet the proper cases for this remedy have not been differentiated.

So also in deafness—some cases have been cured by pilocarpine and others resist its influence—labyrinthine disease and dry catarrhs (Politzer).

Some cases of diphtheria have been recorded where the full effect of pilocarpine has been heralded by the separation of the membrane. But the depression is to be taken into account, and if used the remedy must be carefully watched. At present the use of antitoxin is preferable.

Mumps is often jugulated by this agent in full dose. In diabetes insipidus the flow of urine is quickly lessened by it. Hiccough, asthma, hysteria, hysteroepilepsy, mania, whooping-cough, amblyopia, amaurosis, opacities in the vitreous humor, otitis media, edema of the glottis, the dryness of the mouth in diabetes mellitus and that due to atropine, albuminuria of pregnancy, eclampsia, fulgurant pains of ataxia, hydrophobia, unilateral sweating, and the night sweats of phthisis, are some of the maladies in which this remedy has succeeded. It is one of the best and quickest means of breaking up the chill of malaria. A forming attack of influenza is quickly jugulated by a full dose of pilocarpine, enough to cause free sweating. This alkaloid has been advised for many forms of blood infection, by venomous insects, snakes, even for hydrophobia, and for the effects of such toxic plants as rhus toxicodendron. It has been claimed that pilocarpine will abort an attack of gonorrhea if given at the beginning, before the discharge has become purulent. In all these affections a full dose is requisite, enough to cause free sweating or salivation. It is even advisable to give this remedy in this manner at the very outbreak of smallpox, scarlet fever and measles.

Meltzer and Salant reported a case of strychnine poisoning. A child in the third year had taken an unknown dose. It had been treated by emetics, morphine and chloral to narcotism, but the convulsions grew stronger. As a last resort he was given pilocarpine, gr. 1-24 hypodermically, repeated in eighteen minutes and producing

its full effect. The convulsions ceased within an hour. The authors in their experiments on frogs found that pilocarpine increased the toxic effect of strychnine. This was also true with rabbits. They conclude that recovery ensued in spite of the pilocarpine and not because of it.

W. J. Robinson writes (*Med. Record*): "The use of pilocarpine in the treatment of syphilis is probably not entirely unknown. But the drug is so seldom mentioned in treatises on the subject and it has given the writer such remarkable results in certain cases which refused to be further influenced by the mercurials and iodides, that he considers it a duty to bring it before the notice of the profession in this preliminary note, in advance of a more detailed contribution.

"I have not the slightest intention, of course, to recommend pilocarpine as a substitute for mercury and iodine. But there are certain cases of lues which seem to be supersaturated with mercury and which no longer respond to the drug. We may change the combination of the mercury, we may change the method and avenue of introduction—the symptoms fail to be influenced or become aggravated. The submaxillary, axillary and inguinal glands, instead of diminishing in size under the influence of mercury, as they generally do, become larger and even painful. Such cases are particularly likely to be met with in patients in whom sufficient attention has not been paid to gastrointestinal elimination, to hepatic, renal and dermic activity. Almost every physician has come in contact with such cases in his practice.

Now, try in such cases a few doses of pilocarpine and you will be gratifyingly astonished at the results. Most remarkable is the effect of pilocarpine on salivation and stomatitis. One might think it rather strange to administer a powerful sialogog in salivation. But the fact remains that nothing will stop mercurial salivation so effectually as will small doses—say two milligrams—of pilocarpine. It is much more efficient in this respect than atropine or potassium chlorate. And the rationale is not difficult to understand. Salivation and stomatitis are caused by an excess of mercury, imbedded in the glands and acting as a toxic foreign body. Pilocarpine, one of our most powerful glandular eliminants, and acting both as a sialagog and a diaphoretic, removes the useless excess of mercury, and thus cures the trouble by removing the cause. (Atropine on the other hand merely masks the symptom of mercurial salivation.)

"Another fact of which the writer has convinced himself again and again: Cutaneous syphilides which will obstinately resist the

persistent administration of mercury, will disappear rapidly if pilocarpine be administered for several days, either in addition to the mercury, or even if the mercury be discontinued altogether for the time (provided, of course, the patient has had sufficient mercurial treatment.)

"I explain the *modus operandi* of pilocarpine in such cases as follows: In most cases the greater part of the mercury administered is eliminated through the bowels and kidneys. If the amount to be eliminated is too large or if the ratio of elimination is too rapid, we get cramps and diarrhea on the one hand, and mercurial nephritis on the other. Very little or no mercury is eliminated through the skin and sudoriparous glands, unless special care is taken to keep them at a high state of functional activity. The pilocarpine does just that. The system may be "saturated" with mercury, but the mercury may remain dormant and therefore useless. The pilocarpine increasing enormously the activity of the skin, brings the mercury to the surface, the skin lesions are directly affected and the syphilides therefore disappear. If pilocarpine be given for a week or two and then discontinued, it will be found that much smaller doses of mercury will be necessary inorder to produce the desired effect.

"Pilocarpine should never be prescribed in combination with other remedies—always alone. We can then increase or diminish the dose, or discontinue it altogether, at pleasure. I prescribe the alkaloid either in the form of pills, containing two milligrams each, and of these I order two pills three times a day, sometimes increasing to three or four pills per dose. Or I prescribe it in the following solution:

Pilocarpinæ hydrochlor. .....Gm. 0.12 (gr. 2)
Aquæ chloroformi .....Gm. 120.00 (oz. 4)
Detur in vitro nigro.

Sig.: One to two drams, t. i. d.

"In not a single case have I observed any undesirable by-effects, and in no case could I find, though I carefully watched, symptoms of cardiac trouble.

"I have careful notes of a rather considerable number of cases, in which the beneficial effects of pilocarpine were unmistakable; and I guarded carefully against falling into the *post hoc, propter hoc* fallacy. But I will report those cases at a later date. In the meantime, asking the profession to give pilocarpine a careful trial as an adjuvant in the treatment of syphilis, I will lay down the following propositions:

"1. Pilocarpine is a most remarkable glandular eliminant, and glandular elimination is one of the most important factors in the successful treatment of syphilis.

"2. Pilocarpine is of value in all secondary manifestations of the disease.

"3. There are many cases which become intolerant to the further use of mercury; the system seems supersaturated, and continuing the mercury in such cases means injuring the patient. Discontinue the mercury, giving pilocarpine in interval; this enables us to resume the former drug with excellent effect.

"4. Pilocarpine should be prescribed alone, either in pills or solution, and should be given in doses of 2 to 8 milligrams (1-32 to 1-8 grain) two to three times a day."

In the pilocarpine group we may class seven alkaloids and by it place one glucoside, allied but less closely. Of these, pilocarpine, physostigmine, apomorphine and emetine are best known, muscarine, apocodeine, arecoline and picrotoxin less familiarly. The relation of these agents, their similarity of action and particularities, are best shown in the accompanying table.

It is by no means easy to determine positively the powers of each of these principles from the data supplied by the physiologic investigators, primarily because the principles with which they worked were not always pure, and hence gave variable effects; and moreover the conditions of the animal with which they were making their tests may not have been identical in all cases. For instance, pilocarpine does not cause sweating when the skin is cool, as freely as when it is warm. The effect of veratrine on the ventricles is arrested by low temperatures, as is that of copper, potassium, chloral and ether; but cold increases the effects of strychnine on the spinal cord, if the drug be given in small doses; if large ones are administered raising the temperature increases the convulsions. Picrotoxin is checked or entirely inhibited by low temperatures. High temperatures prevent the tonic effect of digitalis on the heart, by paralyzing the roots of the vagus in the medulla. Many other elements operate to modify the action of even a pure and uniformly-acting drug; such as climate, time of the day, season, conditions of digestion, of the liver and kidneys, and the malady for which the remedy may be given. The matter may be summed up as a complex of difficulties caused by the lack of logical reasoning by the physician. Were we asked what was the greatest deficiency in our system of medical education today we would unhesitatingly reply, ignorance of the laws of logic and their application. We who are

painfully demonstrating the therapeutic principle that two and two make four, get tired seeing our colleagues persistently writing down the sum as five or three.

Nevertheless, as acting in similar conditions, definite remedial agents are uniform in their action, and may be applied with the confidence that springs from certain knowledge. Of this group pilocarpine stands at the head as regards its power of increasing perspiration, saliva and milk secretion; it alone has been shown to stimulate the secretion of earwax, and to cause leucocytosis. It

THE PILOCARPINE GROUP.

	Pilocarpine	Muscarine	Eserine	Arecoline	Apocodeine	Apomorphine	Picrotoxin	Emetine
Sweat—solids	+	+	+			+	+	
water	+	+				+	+	+
Saliva	+ +	+	+	+ +	+	+	+	+
Tears	+	+	+		+	+		+
Respirat mucus	+	+	+		+	+ +		+
Pancreat. juice	+	+	+		+			+
Intestinal juice	+	+ +	+	+				+
Ear wax	+	+						
Bile—glycogen	+	+		+	+			+
urea	+							+
Milk	+							
Urine (solids)	+	+	−					
Suprarenals	+							
Gastric juice	+	+						+ +
All glands	+	+					+	+
Gastric muscle fiber	+	+	+		+		+	+
Intestinal muscle fiber	+	+	+	+ +	+		+	
Bladder muscle fiber	+	+	+ +					
Uterus muscle fiber	+	+	+ +					
Bronchial muscle fiber	+	+	+					
Spleen fiber	+	+	+					
Pupil contraction	+	+ int. local appl.	+	−	−	−		
Pulse	+ −	− −	− −			+	?	+ −
Heart force	+ −	−	+ −	− B	−	−	+	−
Lung force	+ −	− −	+ −	−		+	+	−
Lung rate	−	−	+ −			+	?	−
Arterial tension	− slight	− great	+ −			+ −	+	−
Muscular power	−	−	+ −			−		−
Temperature	+ −	−	+ −		−	?	− + ?	
Muscular irritability	−	−	+			−		−
Intraocular tension	−	−	−	O			−	
Localized action	P. nerve ends	P. N. E.	Cen- (M) ters (O)			Medulla	Medulla	Centers
Excretion	saliva sweat	urine	urine					urine feces
Leucocytosis	+							
Hypnosis		+?			+	+	+	+
Nausea	−	O ?	O		O	− or O		−
Death from			resp. paralysis					
Diarrhea	−	+	+	+ +	+		+	−
Reflex irritability	−	−	−			−	+	−

The + sign means an increase, the − sign a decrease of activity. Where two signs occur in the same column, the first refers to the primary, the second to the secondary effect. O signifies no action, + + signifies a great increase. Cord. C: Medulla. M.

carries away large quantities of urea with the sweat, and here Bouchard's objection to sudorifics in uremia does not apply. He objected that the water thus lost would have carried out ten times more toxins if passing through the kidneys, but it should not be forgotten that pilocarpine removes five times more toxic matter than the normal perspiration does.

No other of the group has been shown to cause leucocytosis, and in this function we have one of the most interesting properties of pilocarpine. This drug has been warmly advocated as a specific remedy in several infectious maladies, such as yellow fever, hydrophobia and scarlet fever. Death from yellow fever is due to the failure of elimination, and pilocarpine may aid by freeing the system of toxins or by combating microorganisms, or both. It is certain that those who have employed this agent in this disease have made very favorable reports upon it. The same applies to its use in scarlet fever; and it may well be that the powerful eliminant and phagocyte stimulation of pilocarpine in the early stages of other infections may exert an abortive power over these attacks. Experiment in this direction has been paralyzed by the dogma of the impossibility of altering the course of any bacterial malady, despite the testimony of those who have studied the biology of the microorganisms. An invasion of the body by a small brood does not cause the disease, but only an invasion by such numbers as overcome the resistant powers of the body. If we can reduce the numbers of invaders or increase the powers of the body, we prevent the development of the disease. Hence the use of nuclein and of pilocarpine, which increase the number and activity of the phagocytes, is in accord with the acknowledged principles of bacteriology.

Pilocarpine also seems most powerful of the group in reducing intraocular tension, and hence is preferable in the treatment of glaucoma. A full sudorific dose will stop any form of itching from jaundice, except that due to hepatic cancer, in which case the relief is only temporary. This action is due to the quick elimination of principles which cause itching while present in the perspiration.

Muscarine differs from pilocarpine in being more depressant, and acting with greatest power on the stomach and bowels rather than on the skin and salivary glands. It stimulates both the secretions and peristalsis of the gastroenteric system, causing free purging and vomiting. It is probably the most powerful of the group as a stimulant of the gastric juice, and of pancreatic, intestinal and hepatic secretion, and possibly as a contractor of the spleen. The difficulty in the use of this alkaloid is that it is so quickly eliminated by the kidneys that it is difficult to secure its full effects unless given intravenously, or in large single doses. This should, however, render it preferable for sudden emergencies, and the absence of lasting depression is notable.

Physostigmine acts less on the secretions but more on the unstriped muscular fibers, especially of the intestines. Its primary

stimulant action is more prominently displayed on the heart, lungs and voluntary muscles, and on the muscular coats of the arteries, raising vascular tension. It increases muscular irritability, and lowers even normal temperature. Cushny pronounces the action of the three hitherto described as purely stimulant of the peripheral nerve endings. Physostigmine shares with muscarine the supremacy in stimulating contraction of the bladder walls. It contracts the uterus so strongly as to endanger the life of the fetus, especially toward the end of pregnancy; and this power is exerted also by muscarine and pilocarpine. All three may in some cases be substituted for morphine in treating habitues, and the patient is unable to distinguish the resulting euphoria from that due to morphine, especially when the habit has endured until passive dilation of the facial cutaneous capillaries has appeared. The effect is not sustained as long as that of morphine, and is lost if the doses are too large or repeated too frequently.

Apomorphine exerts its most decided power upon the stomach when given hypodermically, on the respiratory mucosa when taken by the stomach, in both instances acting quickly as in common with all the members of this group. Its effects as an emetic are due to stimulation of the medullary centers. It is the most powerful stimulant of respiratory secretion and of gastric peristalsis. Much unnecessary dread has been manifested of "green" apomorphine, but abundant experience shows that there is no appreciable alteration in the effects of the remedy. A trace of hydrochloric acid quickly restores the color.

Apocodeine and *arecoline* partake of the general stimulant powers of the group as to the secretory gland cells, all which they incite to activity; but their maximum of power is centered on the intestinal muscular fibers, purgation being the prominent action. They also cause free secretion of gastric juice, intestinal and pancreatic fluids and probably of the bile. Some report that arecoline is superior to pilocarpine in relaxing intraocular tension. Veterinarians have found in arecoline a valuable hypodermic cathartic, administered alone or with physostigmine. This seems to be of interest, since there are many instances where a hypodermic cathartic would be valuable, as when the stomach will not retain ordinary cathartics.

While *emetine* is not usually ranked with this group, it is looked upon simply as the successor of ipecacuanha as an emetic. But the stronger emetic principle of this root is cephaeline, and while emetine is emetic it is a very mild one, and its other qualities

are infinitely more valuable than its emetic powers. Given in doses too small to excite nausea it incites every digestive secretion from the saliva to the rectal mucus, including those of the gastric, hepatic and pancreatic glands. It also stimulates the respiratory mucous secretion. Whether it acts on the milk is uncertain. In overdoses it sometimes gives rise to pulmonary edema like pilocarpine. Huesemann found that emetine caused a cathartic action which could not be obtained from ipecacuanha, in which the crude vegetable matters hinder this action. It has long been recognized that the virtues of ipecacuanha in dysentery are not dependent on its emetic properties but are exerted despite these. In India efforts were made to meet the difficulty by depriving the powder of emetine, supposing this to be the emetic principle; but these proved unsuccessful. But since pure emetine without cephaeline has been produced, doses of one grain may be taken without nausea, if proper precautions are observed.

It should be taken after the patient is lying down in bed, ready for sleep, and he should be cautioned against any movements for half an hour after swallowing it; the dose for an adult is one grain of amorphous emetin, in tablets which should be swallowed whole and without water or other liquid, so that solution and absorption may be as slow as possible. If this is done it is unusual that any nausea is manifested. The patient generally falls asleep within fifteen minutes, sleeps eight hours, and awakes convalescent, to have two spinach-colored stools, the tenesmus gone, the digestive apparatus ready for its functions. In acute alcoholism also, when the patient incessantly craves liquor, and is on the verge of delirium tremens, emetin taken precisely as prescribed, exerts an influence that can only be appreciated when seen. After testing all forms of treatment from opiates, through chloral, bromides, capsicum, feeding, digitalis, etc., the coca wines included, the writer has found in emetin the ideal remedy. The administration and results are as described for dysentery; since adopting this treatment we have allowed no case to develop delirium, or to continue drinking. The patient awakes from the emetine sleep sane, sober and prepared to eat and digest food suitable to his needs. The local irritation described by Wood as caused by emetine has not appeared after these doses of the pure alkaloid employed by the writer, and he is inclined to the view that Wood's emetine consisted largely of cephaeline.

Given in small doses, well within the line of nauseation, emetine is probably the most satisfactory of our remedies for the restoration of normal secretions along the entire digestive tract.

There seems to be a true substitutive action here, as in many forms of indigestion with morbid secretions and diarrhea these are obviated and healthy secretions produced under its influence. In the whole range of the digestive ailments of children we find in emetine all the advantages formerly obtained from ipecacuanha without the distressing nausea that rendered the crude drug so disagreeable to the little patients. This is of greater moment than ever before, since the true Rio ipecacuanha has become so scarce that the last edition of the Pharmacopeia has listed Carthagena ipecacuanha with it, permitting the pharmacist to employ either. The latter is much richer in cephaeline and poorer in emetine.

It is characteristic of the superficiality of our studies of drugs, that no trustworthy data can be had as to the effects of ipecacuanha or its alkaloids on the excretion of urinary solids, or as to their elimination. Surely, before condemning drugs as worthless we might first ascertain what they do in the body, and how they get out of it.

Picrotoxin is placed with this group because it also causes salivation, sweating and vomiting; stimulating the medullary centers strongly and hence slowing the heart through the development of inhibition, lowering temperature (Brunton says raising it), elevating arterial pressure and increasing the rate of respiration. But picrotoxin more quickly and powerfully produces spasms and causes unconsciousness, which none of this group does although emetine disposes to sleep. The relations of picrotoxin are largely with strychnine and digitalin. The properties of this agent and its therapeutic applications deserve study. I know of no more promising field for an investigator in therapeutics.

We see from these considerations that there is in the members of this group a decided similarity of action which is yet far from identity. Under certain limits they may be substituted for each other, but there is room for the exercise of a nicety of choice as to their applications. While all stimulate secretion in general pilocarpine stands at the head as to inducing salivation, perspiration and the flow of milk. Apomorphine is the best emetic, contesting with emetine the supremacy in inciting bronchial secretion. Arecoline is the best cathartic, muscarine the most powerful stimulant of pancreatic and gastric secretion. Muscarine and pilocarpine largely increase the excretion of urinary solids, but the effects of the others have not been determined in this respect. Muscarine also contracts the spleen most powerfully, as well as the bladder, in both cases followed closely by physostigmine and pilocarpine, the

latter acting most powerfully on the uterus. Emetine probably is the best cholagog.

It is probable that the opposition between the effects of small doses and large, primary and secondary action, extends throughout the group, possibly throughout all drug action, and that all these principles strengthen the heart in small doses and weaken it in large ones, all except apomorphine accelerating the pulse. All except picrotoxin, and small doses of physostigmine, lower arterial pressure. Small doses of all increase the force and rapidity of respiration, large doses reverse this. Muscular force is raised by small doses, lowered by large ones, except with apomorphine which depresses it in any dose. The temperature is lowered by all except possibly picrotoxin, but this applies only to febrile temperatures in the case of pilocarpine and muscarine.

That there are other agents belonging to this series seems probable from the following experience: The writer found some mushrooms which he was unable to classify, in any of his books on fungi. They were as large as a dinner plate when fully expanded and nearly three inches thick, and did not show any of the characteristics of the poisonous amanitas. He took one young plant, just ready to open, had it cooked just after being gathered, and partook of a single bite. About an hour later he found himself growing weak, with skin white and cold, sweating, pulse feeble, with no alteration of consciousness or dizziness, pain or suffering of any sort. Vomiting and diarrhea followed of choleraic type, very free, without a particle of nausea or pain. The symptoms subsided within two hours, under moderate doses of atropine, leaving the patient none the worse. The mushrooms were examined in the laboratory but no muscarine could be found. Besides, this agent causes marked pain when given in cathartic doses. It seems that there is in this plant an undetected agent which is the ideal emetocathartic.

Possibly, *nicotine* should have been included in this group, but this body possesses such remarkable and unique qualities that I think it is best studied by itself. It is perhaps the most purely sedative of all remedies, and it is asserted that the human body never becomes habituated to it, even after its constant daily use for a lifetime, but the same dose is as toxic as when it is first taken.

The group as studied is seen to possess agents characterized by their prompt and powerful action, their remarkable safety, dependent largely on the quickness with which they eliminate themselves and other toxins, and the wideness of the field they may fill in therapeutics, which has not been as yet defined. In truth, the

profession seems to have been a little afraid of these principles, notwithstanding the fact that they are almost incapable of destroying human life, in any sized doses. This paper may also be taken as a protest against the pessimistic tendency of some textbooks to give up all attempts at classification or grouping of remedies, and simply arranging them alphabetically.

Pilocarpine is preeminently a remedy for the Burggraevian method of dosage. To an adult it should be given in hot water, in doses of gr. 1-67 to 1-33, repeated every five minutes till the desired effect is manifest. This avoids the danger or inconvenience of an overdose, and as the effects are as quickly shown as when given hypodermically, no time is lost. But when there is question of aborting a dangerous chill give gr. 1-6 by hypodermic. With children, heart cases and weakly adults, give only by the careful method first advised and watch closely. In erysipelas give till slight sweating begins and then enough to keep up this effect. For deafness, alopecia and chronic maladies in general, ascertain the dose requisite for full effect by cumulative administration, and then give this quantity in a single dose at bedtime thereafter.

PIPERINE

Standard granule—gr. 1-6, Gm. .01.

Piperine is an alkaloid from Piper nigrum, black pepper. It is almost insoluble in water, soluble in 30 parts alcohol, 1 part boiling alcohol, very soluble in hot acetic acid, slightly in ether, soluble in chloroform, carbon bisulphide and benzole. When pure it is almost tasteless, on account of its insolubility; but in solution it develops the sharp pungency of pepper.

Like pepper itself, piperine causes a sense of warmth in the stomach, increases the appetite, the digestion, the secretion of gastric juice and the gastric and intestinal peristalsis. Overdoses cause gastroenteritis, as too long or concentrated applications to the skin occasion dermatitis. Doses of 37 1-2 grains caused burning of the eyes, palms and soles, then in all the limbs, with alternate sensations of cold and heat, changing their location. Heart-action was not modified (Neumann and Chiappa). Mosler found that in dogs it caused a decided reduction in the size of the spleen, with slight fall of temperature. Although doubtless eliminated by the kidneys analysis has not detected piperine or the products of its decomposition in the urine.

Piperine has antimalarial properties and has been employed as a remedy for ague but is now used simply as an adjuvant to quinine.

It has also been employed as an internal remedy for hemorrhoids. Colics and diarrheas are relieved by it as by any carminatives; and it forms a valuable ingredient of the powerful mixtures employed to break up by local action the attacks of cholera, dysentery, and congestive chills. In scarlet fever it may be given to stimulate the vitality of the tissues of the throat. In chronic gonorrhea the local stimulus of this agent as eliminated by the urine may arouse the vital resistance to morbific action and thus promote a cure. It will be seen that except in ague the effect is that of a local stimulant and vital incitor; and it is questionable if the oleoresin of pepper is not a better remedy. The uses of piperine other than for this local action have never been studied.

Astringents render piperine inert.

Blom advised piperine in malarial fevers in phlegmatic subjects, with digestive torpor; finding it in them superior to quinine and to salicin. In catarrhal and rheumatismal forms it was contraindicated.

Several authors speak of piperine as stimulating the sexual appetite.

Burggraeve prescribed piperine for chronic discharges. Van Renterghem cured a case of gleet in three weeks with piperine, gr. 1-3 every hour. As a febrifuge the dose may be placed at a grain every hour for an adult. As a gastric stimulant give a grain before meals, to be chewed, not swallowed whole.

PODOPHYLLIN. PODOPHYLLOTOXIN

Standard granules—Podophyllin—gr. 1-67, Gm. .001; gr. 1-12, Gm. .005; gr. 1-6, Gm. .01; podophyllotoxin, gr. 1-12, Gm. .005.

Podophyllin is a resin derived from Podophyllum peltatum, the may-apple. It is soluble in alcohol, insoluble in water. It consists of an inert resinous acid and podophyllotoxin, a white, resinous amorphous powder, very bitter, soluble in diluted alcohol and in hot water. According to Podwissotzky podophyllotoxin consists of picropodophyllin, the true active principle, which is rendered soluble by the accompanying picropodophyllic acid. He therefore prefers podophyllotoxin as the remedial representative of the drug.

Felter and Lloyd pronounce podophyllum a certain but slow cathartic. Small repeated doses short of catharsis induce ptyalism. It increases the bile and intestinal secretions; causes griping, is aided by salt, and does not leave constipation in its wake. Large doses occasion violent emetocatharsis. Overdoses have caused death. When given unnecessarily to improper subjects it has oc-

casioned gastroenteritis. The above-named authors recommend podophyllum for syphilis, rheumatism and scrofula in doses too small to act on the bowels; in atonic dyspepsia, gastric and intestinal catarrh, atonic indigestions, with dizziness, anorexia and heavy headache, indisposition to exertion, dirty flabby tongue, and fulness of the superficial veins, the abdomen and tissues in general; gastric disturbances due to torpid liver; chronic hepatitis; habitual constipation especially if due to portal engorgement (use in small and continued dosage); bilious and malarial fevers (not now so employed); in dropsy, with potassium bitartrate; dysmenorrhea, amenorrhea, incontinence of urine, worms and some affections of the bladder.

Specific Indications.—Fulness of tissues, especially of superficial veins; oppressed full pulse; dirty yellow tongue, and dizziness. Contraindicated by pinched features and tissues, contracted skin and tongue.

These authors treat of podophyllin under a separate head, as a distinct remedy. As a cathartic it requires four to eight hours to purge, and the action may last two days. It maintains a constant moisture of the skin. Alkalies with aromatics check over-catharsis. Trituration with milk sugar increases its cathartic action and renders it less griping. Foods of difficult digestion should not be taken during its administration. Podophyllin is used mostly in small non-cathartic doses as a stimulant to the sympathetic nervous system; acting mainly on the parts supplied by the solar plexus. It improves digestion and blood-making, stimulating normal excretion. "It exerts a peculiarly specific action on all forms of stomach and bowel trouble with atony, characterized by full and relaxed tissues, with mucous discharge;" in summer disorders of children, especially cholera infantum, with mucoid slimy stools; motion sluggish, tongue yellowish white, superficial veins full, face dull; in chronic maladies with feeble digestion, not responding to tonics, usually atony of upper small bowel; for constipation, costiveness of infants or aged; stools hard, grayish white or clayey, floating on water, also for dry stools with tympanites and wandering colicky pains; flatulent colic of children with constipation; dysentery and acute or chronic diarrhea with portal sluggishness, dyspepsia with thickened mucous tissues secreting freely, head full, tissues full and "doughy," veins same, skin sodden, tongue fully coated dirty; cardialgia with constipation; hepatic disorders, biliousness, dizziness, bitter taste, acholic stools, bilious vomiting; acute and chronic hepatitis, hepatic fulness, infrascapular aching, ache in back of

neck, with dizziness; in jaundice with clayey stools alternate with chionanthus; biliary calculi; hemorrhoids dependent on hepatic torpor (alternate with sulphur); cough of bronchorrhea with gastric catarrh; heart disease with hepatic torpor; rheumatism when patient is sallow and inactive, with fulness of tissues, dull pain and heaviness in liver; in renal diseases with the usual indications present; pustular conditions, eczema and cracked or fissured skin (Ellingwood); deep-seated pain in sciatic notch (Scudder); non-intestinal inflammations with constipation; brain disorders and dropsy require large doses as derivative; in malaria alternate with cinchona; cathartic doses are necessary in biliary calculi, apoplexy, dropsy and some inflammations. Younkin advises them in gonorrheal epididymitis.

Ellingwood says this agent is indicated in inactive conditions of the gastrointestinal tract, heavily coated tongue, thick, broad and pale; dirty yellow especially at the base; perhaps vertigo, complete anorexia, and dull, heavy headache; the circulation full and sluggish, abdominal viscera plethoric. Whatever the disease these conditions indicate the employment of this remedy. Always give in doses too small to develop the irritative or cathartic effect.

Cushny says podophyllotoxin causes glomerular nephritis and hemorrhages into various organs when given subcutaneously or intravenously in large doses. This confirms our advice to use podophyllum only in small doses.

Shoemaker recommends podophyllin in sick headache with loose, dark stools; in recurring tonsillitis, etc.

Synergists are euonymin, leptandrin, iridin, which with quassin and caffeine have cholagog properties; purgatives all aid that action of podophyllin; atropine prevents griping and combats the intestinal spasm that hinders purgation.

As a purgative podophyllin is too slow and too violent for use when there are so many better agents of this class. The special indication followed by the writer for years has been its prescription when the stools are dark colored and offensive. Here the dose should not exceed gr. 1-12, given at bedtime, which will act in twelve to fourteen hours. It may be repeated twice a week if needed. We never exceed that dose.

The use of this agent in still smaller doses as advised by the eclectics quoted seem worthy of study and experimentation. Too often we base our ideas of a drug-action solely on its toxic effects and ignore the use of it in doses too small to develop such gross interference with the animal economy.

Podophyllin is variable in strength and it would be wise to substitute podophyllotoxin, which is uniform and the dose is smaller. The only reason this has not been done by American alkalometrists is that the podophyllin furnished the profession is so pure and uniform that the need for a better preparation has not been seriously felt. But if prescribed to be filled by the pharmacist from any podophyllin he may happen to have on hand, it would be better to substitute the more certain form of the drug.

The granules of podophyllin containing gr. 1-67 each are well suited for the uses described by Lloyd. One granule before meals and at bedtime, will suit most cases. The granule of podophyllotoxin is far too strong. One of gr. 1-67 to 1-134 would be quite satisfactory.

POPULIN

Standard granule—gr. 1-6, Gm. .01.

Populin is a concentration from the bark of the white poplar, or American aspen, Populus tremuloides. Poplar bark contains two glucosides, populin and salicin.

Felter and Lloyd say that this bark is tonic and febrifuge, and has been used for ague with benefit. As a tonic it is employed for emaciation and debility, in convalescence; disorders of the reproductive system, impaired digestion, chronic diarrhea, and against lumbricoids; as a diuretic in urinary affections, gonorrhea, gleet, and for granular kidney. It is useful for irritable bladder with tenesmus, if given in very small doses. Webster suggests its use for uterine congestion and for hypertrophied prostate.

Specific Uses.—Marked debility with impaired digestion; tenesmic vesical irritation; tenesmus after urination.

The presence of salicin gives populin a sedative action on the sexual function and appetite which may be useful.

The dose is from gr. 1-6 to 1 before meals and at bedtime.

POTASSIUM BICHROMATE

Standard granule—gr. 1-67, Gm. .001.

Potassium bichromate has been recommended as an alterative against scrofula and syphilis, but is now employed simply as a remedy for some respiratory conditions. The effects are said to be confined to the throat and bronchi, with the larynx, not extending to the bronchioles. Hoarseness and cough are the indications for its

exhibition. These may appear in laryngitis from strain or cold, diphtheria, croup, any inflammation of the region described with tendency to low grades of deposit. It has also been recommended for muscular pains, chronic non-febrile rheumatism, mucoenteritis and acute diarrhea occurring in cold weather (Webster); in chronic diarrheas and dysenteries as a recuperative; and in dyspepsia with yellow coated tongue and gastric catarrh. It should be given at least an hour before meals.

Specific Indications.—Respiratory irritation with hoarseness, harsh or croupal cough, scanty or thick tenacious sputa, difficult respiration, subacute inflammation; low grade inflammatory deposits; mucoenteritis and irritative diarrhea with tenesmus, dyspepsia with gastric catarrh and yellow tongue; corneal ulcers with stringy discharge, croupous conjunctivitis, trachoma with tenacious discharges; non-inflammatory rheumatic or muscular pain; pseudomembranous croup; laryngeal irritation and hoarseness from singing or speaking (Felter and Lloyd).

Shoemaker speaks of this salt as a remedy for tonsillitis where the onset is rapid, tonsils rough, raw and angry looking, with mucopurulent secretions exuding from the follicles, and in non-diphtheritic pseudomembranous tonsillitis; where Weaver considers it a specific.

Abbott recommends this agent as an expectorant, a relaxant in croup and capillary bronchitis, and says that in the third stage of pharyngitis it acts like a charm.

The dose is gr. 1-67 every half-hour to two hours; in croup and capillary bronchitis this dose may be given every ten minutes, in hot water.

POTASSIUM PERMANGANATE

Standard granule—gr. 1-4, Gm. .015.

When brought into contact with any albuminous tissue, permanganate of potassium instantly loses a part of its oxygen. This renders it destructive to the protoplasm with which it comes in contact. The certainty of its decomposition the moment it touches the walls of the stomach has led many to deny the reports of its action in anemic amenorrhea. Nevertheless there is abundant evidence as to its efficacy in this malady. No other preparation of manganese has won repute in this disease; but we have not been able to find any evidence that any other salt of this metal has been sufficiently tried.

A physician told the writer he had discovered a most valuable remedy for phthisis; but that just as he had begun to see the cure of the patients within reach, they were always taken with serious or even fatal pulmonary hemorrhages. It was suggested to him that his remedy was potassium permanganate, and he acknowledged that this was true. The recognition was based on a belief in the power of this agent to induce hemorrhages where due and in these cases it was most likely to occur through the thin walls of the pulmonary capillaries. In amenorrhea the uterus is most apt to bleed, hence its effect in anemic amenorrhea.

Let the patient take iron arsenate during the intermenstrual period, beginning four days before the expected flow to take potassium permanganate in doses of gr. 1-4 every two to four hours, and continuing till the discharge appears or the time is past. If it does not appear it is evident that the supply of blood is insufficient to afford the loss, and this must be made up by treatment and diet.

Potassium permanganate has been used with some benefit in diabetes mellitus, diphtheria, scarlet fever, and other essential fevers, on the theory of its oxidizing powers. In cholera and acute rheumatism its value seems less likely. As a remedy for morphine poisoning it has also been exploited—dose up to full toleration. It has been much used locally. Quite recently it has been reported as checking hemorrhage following circumcision when the child was at death's door, all other treatment having failed. Pure crystals were applied locally.

QUASSIN

Standard granules—gr. 1-67, Gm. .001; gr. 1-12, Gm. .005.

Trommsdorff made an analysis of this plant in 1835 and announced the presence of an amorphous bitter principle. To this Thompson gave the name quassin. From this body Winckler obtained the crystalline form and classed it with the alkaloids. Quassin therefore exists in two distinct states, the amorphous and the crystallized, and it was so demonstrated by Adrian, Moreau and Duquesnel. The amorphous quassin is about ten times less active than the crystallized. This however is not a practical objection with respect to dose, since even in the larger quantity required it is not too inconvenient, the difference being only that between one centigram and one milligram. A more serious objection to the amorphous quassin is its variability, owing to the varying proportions of impurities contained.

Crystallized quassin has none of these inconveniences. It is a pure substance, perfectly definite and identical in composition, always having the same action. Crystallized quassin therefore should be preferred for clinical purposes. Crystalline quassin is prismatic, white, opaque, silky, of micaceous glitter, and permanent in the air. It is inodorous and of very bitter taste, very soluble in absolute alcohol and chloroform, less so in water, and not at all in ether.

In small doses quassin possesses the virtues of the simple non-astringent bitters. Taken into the mouth it increases the flow of saliva, and moderates thirst even during the summer heat. It arouses the appetite. Digestion is hastened, and this seems to be difficult of explanation, since the secretion of gastric juice is not increased or even hastened. Probably it is a secondary effect to the arousing of appetite. But if given on an empty stomach and not followed by food, quassin is followed by a sense of discomfort, and acid regurgitations.

In doses of gr. 1-4 Campardon found quassin to cause severe headache, burning pain in the esophagus and pharynx, nausea, vertigo, restlessness, diarrhea, and ardor urinæ with lessened excretion. Potter states that a concentrated solution caused serious symptoms of narcotism in a child four years old. Its solutions are very destructive to flies and insects, and to ascarides.

Under the influence of regular medicinal doses of quassin the stools become more regular, from the tonic influence of the remedy on the intestinal musculature. Possibly the intestinal secretion is also increased, if there has been deficient secretion from atony. Diarrhea continuing from atony is likewise checked by quassin. Nutrition is furthered indirectly by the improvement in the digestion, not otherwise.

Sousa Refoios found that very large doses injected into a dog caused convulsive tremblings. Haertel applied the alcoholic extract of quassia to wounds of the thigh of rabbits, and found it caused their death.

Kurtz noted temporary paralysis of the posterior extremities in an animal, following lavage of an ulcer with infusion of quassia. The administration of quassia in large doses long continued caused in a man amaurosis (Kurtz), amblyopia (Kraus), and involuntary spasmodic movements in very irritable women (Barbier).

An enema of quassia given an infant caused pallor, small pulse, shallow respiration, debility and vomiting; the life being saved by energetic stimulation (Reckit).

Compardon concluded from his studies of the quassins that they activated and augmented the secretions of the salivary glands, liver, kidneys and perhaps the mammary glands; aroused the action of the gastrointestinal musculature, of the uropoietic apparatus, the bile ducts, increasing the mucous secretions and facilitating the normal excretions; during illness they increased the appetite, renewed the forces, facilitated normal excretion, rendered defecation easier, and hastened the expulsion of renal and of hepatic calculi; with healthy as well as sick men they determined in a certain dose toxic effects recalling the action of the strychnine group; amorphous quassin in doses above 2 1-2 grains, and the crystallized in doses above gr. 1-4, caused symptoms of intoxication, local or general, such as nausea, vomiting, diarrhea, vertigo, febrile agitation, cramps, and convulsions, for which it was necessary to use chloral internally and chloroform externally (by inhalation?).

Physiologic Action.—Houdé says quassin does not act directly on the assimilation but acts by stimulating the appetite and digestion, and in this manner improves nutrition through the quantity and quality of the food-elements absorbed. This action of quassin is of great importance. The immediate effect following the ingestion of quassin is an increase of salivary secretion, which however preserves its normal composition. This effect very soon is followed by an imperative desire for food which it is best to satisfy at once if we are to avoid the sensation of pain in the stomach together with acid regurgitation and even a sense of exhaustion sure to follow if this demand is not satisfied.

Quassin increases the formation of ptyalin, or animal diastase, which is so necessary for the digestion of starchy matters. This ptyalin does not exist in the saliva which flows from the Stenson and Wharton ducts, but originates from the buccal mucous surface by a change of the salivary product on coming in contact with the air. The saliva of the glands and of the secreting ducts is therefore inactive, not ready for transforming starchy substances into glucose, while the mixed saliva which flows about in the mouth determines this chemical decomposition of the starches at once. From this it follows that the physiologic rôle which the saliva plays in the digestion is an important one and that the action of quassin is a powerful factor in the first phase of that process. The action of quassin extends from one end of the digestive tube to the other. Its action is that of a pure bitter, that is, one which stimulates all the secretions of the intestinal tube, salivary, gastric and intestinal. This primary action is accompanied by a tonic action on the muscular fibers.

This physiologic action on the secretions of the digestive tube is of considerable importance clinically. The appetite is aroused, digestion improves and is more complete, and intestinal stasis is obviated by improved peristalsis. These results are due to the fact that quassin does not render the secretions more abundant at the expense of quality, but while increasing their volume, preserves their normal quality and composition. It is therefore perfectly natural that it does not only sharpen the appetite but also facilitates the primary and secondary digestion and prevents constipation.

Quassin stimulates the liver, as it does all other glands of the digestive tract, augmenting its normal secretion and so contributing its share to the assimilation of the ingested food. In the same way quassin acts on the pancreas, this also resulting favorably to nutrition. Moreover, this action of quassin on the liver facilitates the expulsion of a biliary calculus in hepatic colic, while by increasing the flow of bile it tends to diminish the size of the liver in biliary congestion.

Quassin augments the amount of urine to double and treble its normal quantity, and to this action is joined increased muscular tonicity of the urinary apparatus, which is a corollary to the tonic action on the intestinal muscular fibers. Under the influence of quassin the expulsive muscles of the urinary apparatus are stimulated promptly and energetically. This augmentation of the urine and the tonicity of the expulsive muscular fibers makes of quassin a useful remedy in nephritic colic the same way as in hepatic colic.

Compardon speaks of quassin as capable of stimulating the lacteal secretion in nursing women. The action of quassin on the intestinal muscular fibers makes it valuable in combating the formation of gases in the intestines and the resulting disagreeable borborygmi. The same action of quassin makes it useful in the nervous vomiting of pregnancy. Quassia decoction and quassin act destructively on the parasites, such as the ascarides, lumbricoids and oxyures. In a word, quassin localizes its action in the digestive canal and is indicated in a great number of affections which here have their seat.

In digestive troubles the question is nearly always about errors of diet. In these sins against hygiene every individual digestive tube reacts in its own way, according to the importance and nature of the present alimentary error, the previous vigor of the subject and the condition of his nervous system. In the initial state the noxious action keeps up an exaggerated reaction, a general hyper-

functionating of the digestive tube. This hypersthenic period is owing above all things to the diet, and in fact comprises those dyspepsias that are most easily cured. But in an advanced stage, and sometimes even at the beginning, the digestive forces stagger at the task imposed upon them. There supervenes a gastrointestinal hyposthenia, hyperchlorhydria, hypopepsia, abnormal dilations and fermentations, then intestinal atony, flatulence and ptoses mark the localized incapacity of the digestive system to elaborate the material presented. At first a limited allowance of the alimentation may parry this general deficiency, but a little further on such underfeeding can not be safely kept up with organs overworked.

But whatever the diversity of symptoms may be in all these affections they all have one common bond. The digestive canal appears from beginning to end as one mass of glands which secrete the juices needed for digestion under the continuous influence of muscular contractions which keep up the secretion. Thus is gastrointestinal hyposthenia at the base of nearly all dyspepsias, characterized on the one hand by debility, distension, feebleness of the musculature of the digestive tube, and on the other hand by insufficient secretions of the glands, a relative or absolute acrinia.

This state of things may be preceded by a period of muscular spasm and glandular perversion of action corresponding to the reactionary condition. It may be followed by an inflammatory and infectious period of the mucosæ, which may be grave and final. But the period of muscular atony and hypocrinia comprises the great majority of dyspepsias that come under medical treatment.

The above conception of the subject has the advantage of simplifying the therapeutics or rather of precising the indications to be fulfilled.

Gastrointestinal hyposthenia demands evidently severe dietetic treatment. There may be a demand for various prescriptions according to phenomena peculiar to certain localities of the canal, but there are always two grand indications dominating here therapeutic effort: tonify the musculature, stimulate the glands—favor peristalsis and the gastrointestinal juices.

What influence can we exert over the smooth muscular fibers of stomach and bowels—have we any agent capable of stimulating the glandular secretion? Yes!

It is enough to remember the very particular action of quassin in this respect. There is no medicament that has such a direct and marked effect upon the peristaltic contraction of the smooth muscular fibers of the digestive *primæ viæ*. There are purgative and

cathartic agents which affect the lower portions of the intestines whose action is purely that of unloading, and they operate where the glands are rare. Quassin on the contrary stirs up the contractions of the stomach and of the small intestines, and this is always accompanied by a noticeable hypersecretion of all the glands. Is this second action independent of the first or is the augmentation of the secretions a simple result of the more vigorous peristaltic action? Practically the point is of little importance, and yet this secretory power of quassin is so marked, extending as it does to all glands, including both the salivary and intestinal glands) that the tendency is to attribute this secretory property to its having a particular action on the glandular elements.

And thus quassin fulfills perfectly the two indications of gastro-intestinal hyposthenia. It is not necessary now to seek further for the reason that quassia wood, in years gone by, had such popularity in the treatment of dyspepsias.

Quassin associated with proper dietetic treatment gives remarkably effective results in all those cases which we call gastrointestinal hyposthenia, anorexia, gastroectasis hypochlorhydria, atonic dyspepsia, flatulencies, enterocolitis, constipation and diarrhea from intestinal inertia, biliary stasis, splanchnoptosis, etc.

Therapeutics.—Quassin has been employed largely for the purpose of stimulating digestion and the flow of bile. It is indicated, says Van Renterghem, in labored and slow digestion, stomachal and intestinal, in all morbid states accompanied by defective biliary secretion, in chronic intestinal catarrh due to the presence of badly digested food, and in lienteric cases. He prefers the granules of gr. 1-67 each, silver coated, to cover the bitterness; and as an eupeptic gives one or two to an infant, three or four to an adult, a little before the principal meals. Burggraeve loved to associate with quassin the arsenate of soda, in like doses, and this combination is a happy one. The salts of arsenic in the small doses increase the appetite, activate the digestive functions, and act as antiputrefactives. This is their direct action, but their rôle is not ended here. From the moment they enter the circulation they exercise their modifying action on the nutrition, tonifying the tissues, and preventing the impoverishment of the blood, thus indirectly contributing to the cure of the dyspepsia.

As a cholagog, Van Renterghem prescribes quassin in doses of a granule or two every hour, alone or with caffeine, podophyllin, euonymin, iridin, leptandrin or sodium sulphate. In lienteria the best auxiliary is surely magnesium sulphate in purgative doses,

given in early morning, followed according to the indications by naphthalin, bismuth subnitrate, cotoin, strychnine, hyoscyamine, etc.

Like all the bitters quassin has some good influence in remittent and intermittent fevers. It preserves animal matters from decay. It has been employed as a remedy for alcoholism; and to destroy the appetite for liquor.

In France quassin forms one of the ingredients of the liquid served as a beverage to school children, which contains also licorice and a trace of phosphoric acid; the object being to discourage excessive drinking in summer. This effect of relieving thirst has not received the attention it deserves on this side the Atlantic. The French dosimetrists also employ quassin to a large extent as a general toner and vital inciter where we use the unnecessarily powerful strychnine—and here we might with advantage follow their example, holding strychnine in reserve for emergencies worthy of its powers, and discouraging the popular tendency to make of it a stimulant for lay self-prescribing whenever such an agent is supposed to be needed. Strychnine should be held strictly in the control and possession of the physician.

We cannot agree with our French brethren as to the best manner of administering the bitters. A quassia cup imparts its bitterness to water for years even if used every day. The quantity of quassin dissolved at each dose is exceedingly small, or the cup would soon be exhausted. Yet the therapeutic effects are undeniable; and in fact seem to be better than when quassia is swallowed without being tasted. The effect upon the gustatory nerves, if not the principal one, is at least too important to be disregarded. Give the smaller granules of quassin, which are powerful enough for all ordinary cases, and let each dose be taken in solution just before each meal; and you will secure the maximum effect with the minimum of the remedy.

The use of quassia infusions as a remedy for seat worms should be discouraged. There are more efficient methods of treatment, devoid of the danger sometimes accruing to the use of quassia.

As a remedy for the alcohol habit the simple bitters are less effective than berberine, which more powerfully tonifies the relaxed fibers and removes the depression and nervelessness of the reformed inebriate. But when the habit has been broken it is a good thing for the reformed man to carry in his pocket a vial of quassin granules and employ one as a lozenge just before going to meals.

QUININE

Standard granules—Arsenate gr. 1-67, Gm. .001; gr. 1-6, Gm. .01; hydrobromide gr. 1-6, Gm. .01; hydroferrocyanide gr. 1-67, Gm. .001; hypophosphite gr. 1-6, Gm. .01; picrate gr. 1-6, Gm. .01; salicylate gr. 1-6, Gm. .01; sulphate gr. 1-6, Gm. .01; valerate gr. 1-6, Gm. .01.

Quinine is an alkaloid from the bark of various species of Cinchona. Closely allied bodies are found in Remijia, and in other plants. Cushny enumerates as constituents of the cinchonas 21 alkaloids, 6 acids and 3 neutral bitter substances. The effect of each specimen of the bark and of the galenic preparations derived from it, consists of the sum of the effects of such of these active principles as it possesses, in the quantity and relative proportions in which they happen to exist in that particular specimen. Those principles which have been studied agree as to their general effect to a remarkable degree—in fact we doubt if there is a parallel case in the known vegetable materia medica, where all the active principles of a plant have general effects so closely similar. But few of these active principles have been studied or even tested; so that in the numerous agents of unknown powers there may be as absolute antagonism as exists in the alkaloids of opium, hyoscyamus and jaborandi. The presence of three varieties of tannic acid accounts for the astringency of cinchona and the slow action of the crude preparations. Great efforts have been made by the Indian government to push the use of a preparation consisting of the combined alkaloids from the plant, but it has scarcely been heard of outside that country, the medical profession being satisfied with the convenience, certainty, smallness of dose, quick action, palatability, and other advantages which quinine possesses over the bark from which it is derived. That the thought of obtaining similar advantages from the use of the alkaloids of other plants comes so slowly to the mind of the profession must be set down to the intense conservatism characterizing it.

Physiologic Action.—Quinine first stimulates, then kills protoplasm. Binz found that minute doses may increase the movements of amoeba and infusoria, at first; larger doses paralyze them at once, the protoplasm becoming dark and granular. On the germs of putrefaction the effect is about equal to that of carbolic acid. Alcoholic, lactic and butyric acid fermentations are retarded or prevented by quinine. Moulds, however, grow freely in its solutions. Experimenting with the sea-urchin, Hertwig found that quinine paralyzed the movements of its spermatozoa, and delayed or prevented the evolution of the ovum. Minute quantities of

quinine suffice to stop the movements of the leucocytes, prevent their passing through the vessel walls, and cause them to become darker, granular, and to break up into debris (Binz). No accumulation of leucocytes at an irritated point occurs under quinine, and if the irritation has preceded the application of quinine, the process is at once arrested by it. The same result follows when quinine is carried to the part by the blood vessels. Ordinary doses of quinine lessen the number of leucocytes in the blood.

The oxidizing action of blood is diminished by quinine. So is its coagulability. The gastric and pancreatic ferments are rendered less active by quinine (Rossbach), but ptyalin and diastase are unaffected (Binz). Quinine prevents the formation of hippuric acid from benzoic acid and glycocoll. The functions of the spinal centers, respiration, circulation and vascular pressure, are all stimulated by small doses of quinine and sedated by very large ones. The arterioles are contracted, the heart accelerated, both actions being reversed later by large doses. The same preliminary stimulation and subsequent depression is noted as to the muscular fiber. The urine is slightly increased.

Given to man in medicinal doses, quinine acts on the stomach as the other bitters do, increasing the appetite. Full doses cause ringing in the ears and some deafness; total and permanent deafness has followed a single dose of 40 grains, but this is exceptional. The field of vision may be contracted, and partial or total blindness may ensue, lasting for days or weeks.

Williams describes a case of quinine amaurosis. A woman, age 22, in good health, at 8 p. m. took eighty grains of quinine sulphate. At 10 p. m. she was in a stupor, at midnight nausea and vomiting occurred. The next morning she was blind. Three days later vision commenced to return, but eighteen months afterwards was still very defective.

Color vision is often affected. The aural disturbance is attributed to congestion of the auditory apparatus, that of sight to contraction of the retinal vessels, which may be followed by some optic nerve atrophy. Large doses cause a sense of fulness in the head, slow pulse and staggering. In the few cases in which overdoses have proved fatal, there were symptoms of heart weakness and collapse, loss of sight and hearing, muscular weakness, apathy, slow, gasping respiration, and coma with failure of respiration Delirium and convulsions have been reported. The toxic dose is uncertain, since an ounce has been taken without dangerous symptoms. Idiosyncrasies are not rare. The aural and ocular symp-

toms described occasionally follow the use of small doses; many varieties of eruptions have been attributed to quinine; and a fever resembling malaria. Sometimes it contracts the uterus and may cause abortion, though as a rule no such effect follows the use of even full doses. It often irritates the stomach, even in moderate doses—as all the bitters are liable to do—and may cause diarrhea, albuminuria or hematuria. The writer had one patient in whom four grains of quinine repeatedly caused purpura hemorrhagica.

Even in doses too small to cause any tangible symptoms, quinine affects metabolism. The destruction of nitrogenous tissues is markedly lessened, the production of urea and uric acid being especially restricted; the excretion of phosphates and sulphates is also reduced, but the excretion of carbonic acid and absorption of oxygen through the lungs is not materially altered. Cushny concludes from this that the work done and the heat formed are not affected but that the death, growth and repair of the tissues are less active. Nitrogen is stored in the body.

In malarial and other fevers quinine lowers the temperature by direct action on the tissues (Binz). It has little effect on a normal temperature. Gottlieb found both the production and the radiation of heat reduced by quinine. The reduction of temperature is much greater if given when the fever is falling, than when it is rising.

Quinine appears in the urine within thirty minutes from its administration by the mouth, and one-half the whole dose is excreted within six hours (Cushny). Traces are still to be found seventy-two hours after it has been taken.

Solutions of a grain to the ounce destroy microorganisms, and double this strength prevents fermentation and putrefaction. Large doses destroy the sense of hunger and arrest the secretion of gastric juice. Quinine has been detected in the sweat, tears, and the milk of nurses; in bile and the fluid of dropsical effusions. It is also found in the feces. Inflammatory degeneration of tissue is notably decreased by it. It probably destroys infectious microorganisms in the blood and tissues (Shoemaker).

The sulphate of quinine is soluble in 800 parts of water, the hydrochlorate in 35, the hydrobromate in 54, and the valerate in 100. The bisulphate is soluble in 10 parts of water. The addition of sulphuric, hydrochloric, hydrobromic, or any acid, renders the sulphate more soluble, but increases the bitterness of the solution. Quinine is absorbed from the rectum, the vagina, or the subcutaneous tissue, though the latter is a very painful method of administration and apt to be followed by abscess.

Piorry, Paget, Magendie, Landois and Mosler affirm that quinine reduces the size of the spleen even in health, as it undoubtedly does in malarial affections, but Cushny finds the evidence inconclusive.

By many quinine is credited with the power of checking the exudation of fibrin, and for this reason it is administered in full doses to prevent the exudations of croup and pneumonia. Whatever the reason, the method possesses merit.

Synergists.—As an antizymotic, quinine is aided by arsenic, salicylic acid, resorcin, and the sulphocarbolates; as an antipyretic it is associated with aconitine, veratrine, digitalin and the coal tar group; the strychnine group increases its tonic and febrifuge effects, while as a means of delaying or preventing nitrogenous waste it is aided by caffeine and by alcohol.

Incompatibles.—Tannic acid, iodine and its salts, alkalies and their carbonates, the alkaline earths, all precipitate quinine from solution.

Therapeutics.—The most important use of quinine is as a remedy in malarial fevers. Here its great value has led to abuse and incredible carelessness in its administration, so that a series of reactions against it have occurred.

In all cases when time is allowed it is best to thoroughly empty the alimentary canal by efficient cathartics, and disinfect with a sufficiency of the sulphocarbolates. Then give quinine in full doses, during the decline of the fever. In intermittents from 10 to 15 grains a day suffice for an adult; in remittents these doses should be doubled; while in the pernicious forms of malaria met in the tropics forty to sixty grains should be given without delay. It is best to use the soluble salts, as much of the large doses of the sulphate is ejected unabsorbed. In the algid forms, or pernicious chills, the dose should be injected hypodermically or into the rectum, in solution. Inunctions of quinine are too uncertain for dependence. The bimuriate of quinine and urea is quite soluble, but the hydrochlorate answers about as well.

It has been claimed that the arsenate of quinine fully represents the virtues of this agent, and that a grain equals in therapeutic effect fifteen grains of the sulphate. This is still undecided, but there is reason to believe that it is true. At least the efficacy of the arsenate in the chronic forms of malarial toxemia appears to be much greater than that of the sulphate, in any dose. It is hardly possible to overestimate the importance of the preliminary cleansing and disinfection of the gastrointestinal tract.

Many prefer to administer the antipyretic dose of quinine in a single dose, aiming to so give it that ringing of the ears may occur at or just before the expected recurrence of the chill—that is, about six hours before the latter is due. But the writer believes any advantage derived is suggestive, and malaria has always been known to be anenable to suggestion. Better results may be obtained with much smaller doses by giving the quinine in very small doses very frequently repeated, so that there is never a moment when the remedy is absent from the blood and the alimentary canal.

No matter how large a dose of quinine may be given, it will not prevent the multiplication and continued action of the parasites after the effects of the dose have subsided; but if there is a continual infiltration of the drug into the blood there is never a moment but that the newborn plasmodia are met and killed by it; until the invaders have become extinct. This at least illustrates the method of treating the disease that has proved most successful, whether the explanation is literally correct or not.

Van Renterghem advises the administration of a massive dose to break up the attack; meeting the fever with the defervescents, following with the selected quinine salt, one to five granules every half-hour, or hourly, adding a granule or two of strychnine for adults or one to five of brucine for children. This is continued until the next period for a chill has passed. If a new access occurs strychnine is given alone, a granule or two every half-hour during the cold stage, then the Defervescent Triad during the fever. But the second chill is unlikely to happen, the third still more so. On the free days one should take the arsenates of quinine and arsenic, one to three granules each, every two or three hours. This dosage is not absolute—the physician must regulate it by the need and the effect. Dosimetry gives a choice of the quinine salts.

In malarial dropsy and enlarged spleen he employs quinine and such other agents as may be indicated—iron for anemia, quassin for anorexia and dyspepsia, strychnine for general systemic atony, digitalin for dropsy, quinine and arsenic for the paludal cachexia. Of the arsenates of strychnine, iron, quinine and soda, give five to ten granules each in a day; quassin two to four granules before each meal; digitalin a granule or two hourly or half-hourly till the urine is secreted abundantly.

In neuralgias and paroxysmal neuroses quinine will often prevent the attacks. He prefers the hydroferrocyanide, valerate and arsenate here; given half-hourly or hourly in the intervals, often adding strychnine arsenate. During the attack give aconitine,

caffeine, morphine, hyoscyamine, strychnine, gelseminine, butyl-chloral or zinc cyanide, singly or combined, as the symptoms determine.

For non-paroxysmal neuroses, quinine has not the decided beneficial action shown in the periodic forms.

As an antipyretic quinine has been largely employed in many fevers, typhoid, eruptive, pneumonic, pyemic, hectic and puerperal; alone in massive doses or with cold baths. Juergensen gave doses of 60 to 75 grains in pneumonia, and Pepper gave suppositories of ten to twenty grains in the pneumonia of infants. In the fever of tubercular phthisis the old favorite termed Niemeyer's pill may be represented alkalometrically by a grain of quinine hydrochloride, digitalin gr. 3-67, emetine gr. 1-67, and codeine gr. 1-12; and this may be given every four hours. But cleansing and disinfection of the alimentary canal has proved more effective, with the Defervescent Triad or the Trinity of Burggraeve, so that the need for quinine is rarely met.

In acute inflammations of all sorts Van Renterghem considers quinine indicated as an antiphlogistic. He advises small doses repeated so often that the solution of quinine constantly bathes the affected tissues. He has also employed this agent with success in treating hemorrhages, bronchial, pulmonary, intestinal and uterine; giving fractional doses with arsenic, strychnine, ergotin, and of late with hydrastine.

As a general tonic quinine has been altogether replaced by strychnine.

Quinine is one of our most reliable remedies in whooping-cough, when given in doses of three or four grains to a child two years old. It is best given here as the sulphate, suspended in syrup of yerba santa, which covers the taste admirably. There is possibly some local action on the throat when thus given. The addition of acid to render the quinine soluble ruins this mixture by precipitating the yerba santa as a tarry mass.

In true spasmodic asthma a full dose of quinine, gr. 15, given at bedtime, will quite surely prevent the paroxysm for the following night.

As quinine lessens the production of uric acid, part of the credit it once possessed may have been due to its administration in uric-acidemia. But agents promoting the elimination of this toxin are to be preferred.

Quinine has been advised in the choleras, presumably as an antiseptic; but there are many better and less irritant agents.

Lustgarten exhibited a case of lupus erythematosus practically cured by the use of quinine. The dose was ten grains a day, gradually rising to thirty grains, continued indefinitely.

Shoemaker says quinine favorably influences the bronchopneumonia of measles, and combats the tendency to caseous degeneration; reduces the discharges of suppuration, prevents sapremia and pyemia; is of use for phthisical night-sweats, neurasthenia, general debility; Meniere's disease (Charcot); and malarial skin diseases (Yandell).

Forchheimer employs quinine in exophthalmic goiter. He says: "My favorite method of treatment which I have employed for over twenty years is as follows: It consists in the continuous use of quinine hydrobromide, with or without ergotin. This salt was chosen because it is better borne by patients than the other salts, i. e., cinchonism is not so easily produced. As will be seen, my experience has been very extensive in the use of this drug.

"Quinine hydrobromide is given in doses of Gm. 0.3 in gelatin-coated pills, four times daily; to each pill is added ergotin, Gm. 0.065, when the quinine alone does not give results in forty-eight hours. As these pills may have to be given for a great length of time, I may here say that I have never seen any bad permanent effects follow their administration; one of my early patients took four of these pills daily for nearly three years without detriment to herself. The effects of this method of treatment are as follows: First the tachycardia disappears, then the thyroid gland diminishes, and finally the tremor and the exophthalmos. The first change takes place usually after the treatment has been used for forty-eight hours; it should then be continued until all the symptoms have disappeared; in the fully developed cases this result has been reached in as short a time as four months and as long a time as three years.

"In the treatment of twelve fully developed cases I have had only three failures; in abortive cases there have been less. I do not take into consideration the number of cases I have seen in the last three years, because relapses may occur up to this time. The failures were in that class of cases which may be called the foudroyant form, originally so or developing as such in a relapse. Occasionally, however, a case is found in which there is no apparent reason why the treatment should not succeed; however this may be, nine of my original twelve cases have been without any symptoms for at least three years and may be considered perfectly cured. I have seen a large number of cases of the aborting form, especially

those developing during or after the menopause, improve under this treatment in from four to six days, so that the whole clinical picture was changed.

"On account of the general condition—the extreme nervousness of the patient, for instance, or the state of the heart—it frequently becomes necessary to supplement this method by the Weir Mitchell treatment.

"In order to test whether the recovery is complete it is only necessary to withdraw the quinine; if symptoms do not return in two weeks the patient may be considered cured. How the quinine acts it is impossible to say; it may act indirectly upon toxic bodies in the blood, by slowing the heart, by contracting the arterioles, or by stimulating inhibitory centers. At the time of writing I have treated forty-one cases of Graves' disease with this method, with five failures."

Dr. Forchheimer does not state how long he continued the ergotin in the cases requiring it; probably until the subjective symptoms largely disappear. One of our correspondents found the ergotin necessary in two cases but was able to discontinue entirely its use in one month.

Haig states that ordinary sulphate of quinine contains 20 per cent of xanthin, equivalent to uric acid, and this may aid in destroying red blood cells and liberating hemoglobin, producing hematuria in malaria.

Quinine was for many years employed so generally that it was almost a matter of course to have this alkaloid in the prescription; and many tons of it were thus wasted. Its place in this respect seems to have been taken by strychnine.

The contraindications for quinine are: Idiosyncrasy, acute inflammation of the genitourinary tract, kidneys, stomach, bowels, or middle ear with impaired hearing, infantile eczema, epilepsy.

The effect of quinine upon the ears is largely prevented or relieved by giving full doses of any bromide, or of hydrobromic acid. The use of small and oft-repeated doses allows the physician to administer this drug till the first evidences of action are manifest and then stop it or give less frequently; by which all such unpleasant effects are prevented.

Some authors credit quinine with oxytocic powers, and advise it in place of ergot in atonic states of the uterus. This would render pregnancy a contraindication to its use. But others deny this, and look upon such an action as rare, and an idiosyncrasy. In dealing with pregnant women it is well to keep on the side of safety.

Quinine hydroferrocyanide may be considered as a compound of hydrocyanide of quinine and cyanide of iron. It has the formula, $C_{20}H_{24}N_2O_2(CN)_6Fe_2H_4+3H_2O$. It is not necessary here to enter into the process of manufacture. Dr. Burggraeve resuscitated the remedy, and following the master, Van Renterghem tried it, first upon himself and then upon his patients. He found that the small dose which is sufficient to check an attack of intermittent fever had no appreciable influence upon a healthy person. Moreover, in the small dose, it is as efficient as quinine sulphate in the larger dosage.

The remedy possesses antiperiodic, antipyretic, sedative and reconstituent virtues, which it derives principally from the quinine and hydrocyanic acid; in part also, perhaps, from the iron. The cyanide of iron was for a time employed in medicine, but is not now used. It was tried in intermittent fever, epilepsy, facial neuralgias, and, externally, in sanious ulcerations; it was also recommended as an antichlorotic and sedative in anemias with exaggerated nervous irritability, but it was abandoned (1) because the results did not justify its use, and (2) because of its insolubility in the gastric and intestinal juices.

The first of these reasons is better than the second, for clinical experience is what decides the value of a remedy, while the question of solubility or insolubility is not so important as one might believe. It is conceded that the more soluble a remedy is, the more readily it is absorbed, yet the truthfulness of the sentence, *Corpora non agunt nisi soluta* (bodies do not act unless they are dissolved), we shall accept only relatively.

For instance: It was once believed that alkaloidal tannates must be inactive because of their insolubility in the liquids of the system. But, later it was shown that tannate of quinine exercises its therapeutic effect, though tardily. Also, sulphide of mercury is apparently inert, for fifteen Grams of it spread over an open sore or introduced into the stomach of a dog produces no effect; yet cinnabar has been prescribed successfully in the scrofulous and rachitic diatheses. We do not yet know sufficiently well the conditions which determine the possibility or the impossibility of the absorption of a remedy.

It does not, therefore, seem unreasonable to us that cyanide of iron, insoluble and inactive though it may be when administered alone, may become soluble and active when combined with quinine cyanide. We shall retain this opinion until a better one is shown.

This remedy, says Dr. Van Renterghem, has given wonderfully good results: (1) As an antipyretic and antiperiodic in intermittent fevers, and in typical neuralgias; (2) as a defervescent during the febrile period of various maladies; (3) as a sedative in the coughs of whooping-cough, and in the first part of the course of phthisis: (4) as a tonic and blood reconstructive. It is above all as an antifebrile and antiperiodic agent that it gives the most remarkable results.

Van Renterghem quotes in detail a large number of illustrative clinical cases, from which we have selected a few:

A Case of Tertian Fever.—N. O. S., mayor of the village, age 60, had two attacks, recurring at the same hour. The next attack was expected the following morning at 8 o'clock. He was given 0.6 Gm. (gr. 9) of quinine hydroferrocyanide, 0.03 Gm. (gr. 1-2) of strychnine arsenate, and 0.3 Gm. (gr. 5) of white honey. This was divided into sixty pills and three were given five hours before the expected attack, to be followed by three every hour until the hour of attack. The following day there was an attack, but lighter; the day after this none appeared, and from this time none occurred.

A Case of Quotidian Fever.—Mrs. S., age 55, in feeble health, had five successful attacks, fever preceded by chills. She was given the same treatment as the above and after this the fever did not recur.

A Pediatric Case.—This was the youngest son of the author, thirteen months old. He was well during the day, but during the night the mother noticed that he was restless and in the morning covered with perspiration. At 10 p. m. he had a fever of 39° C. (102.2° F.), falling in the morning to 37.4° C. (99.3° F.). A diagnosis of quotidian intermittent fever was made and the following prescribed: Brucine, ten granules; quinine hydroferrocyanide, twenty granules; sugared water, twenty teaspoonfuls. Dissolve and give a teaspoonful every half-hour, commencing at 8 a. m. (The brucine granules contain gr. 1-134; the quinine hydroferrocyanide granules, gr. 1-67.) This prescription stopped the fever the first day, but was repeated during the next three days.

Tertian Intermittent Fever.—D. R., the son of a laborer, had had three attacks, the first at 1 p. m., the second at 10:30 a. m. and the third at 8:30 a. m. He was given magnesium sulphate on an empty stomach in the morning, and quinine hydroferrocyanide was given as in the first case. The next attack was expected March 29, at 6 a. m., but did not appear until 9 a.m., and then the severity was much modified. March 31 there was no attack and cure was thereafter complete.

Double Quartan.—C. M. V., a robust peasant, was seen first March 1. He has suffered from fever for the last three months, the attacks coming regularly two days in succession every three days. The attack following the free day was less severe than the other. The fever begins with *cutis anserina*, always at 6 p. m., and lasts all night. Appetite good and no pain in left hypochondrium, though the spleen was enlarged. On the fever day two granules of quinine arsenate and two of strychnine arsenate were given every hour from 6 a. m. to 8 p. m., making fifteen doses. Treatment was commenced on March 1 and on the fourth, the free day, the patient said, although the fever had continued: "I can see very well that there is something in the little granules; I seem to have more strength; then, too, my face gets rosy in the evening, and as if on fire."

He was then given quinine hydroferrocyanide, Gm. 0.3 (gr. 5); strychnine arsenate, Gm. 0.02 (gr. 2-6); white honey, Gm. 0.15 (gr. 2 1-2). This was made into thirty pilules, of which fifteen were to be taken on the fever day, say one every hour. The fever not yielding, the quantity of the hydroferrocyanide in the prescription was doubled on the seventh, with the result of preventing the attack the following day and partially aborting that of the day after. Thereafter there was only one slight attack, and soon the quinine salt was reduced in quantity to the amount in the original prescription. The cure remained complete up to the end of December, when the report was made.

Following this come other reports of various malarial fevers; for instance, one of a chlorotic girl of fifteen, cured of a double quartan after massive doses of quinine, given in the usual manner, had failed. In this case the arsenate, the hydroferrocyanide and sulphate were given. A tertian in a man of thirty was readily cured by the conjoint use of quinine hydroferrocyanide and strychnine arsenate. Another case in which gigantic doses of the sulphate failed to effect a cure, was cured by Van Renterghem by the same method.

Of special interest was a case of *Pernicious Intermittent.* This occurred in a girl ten years old, who was first seen on June 6. The morning before she had a chill followed by fever, which had been continuous. She complained of dull pain and tenderness in the splenic region. Spleen enlarged. The pulse was 150 and the temperature 40° C. (104° F.), while respiration was rapid, shallow and irregular. Pain in the chest, though examination showed no abnormality. Stools were retarded; urine scanty and of disagree-

able odor. This was the fourth attack which the child had had. The diagnosis was pernicious intermittent with pulmonary congestion.

The bowels were cleaned out with magnesium sulphate and the fever sedated with veratrine and aconitine. In addition the quinine hydroferrocyanide was given, five granules every hour until 10 p. m. If fever did not recur the quinine and strychnine were to be resumed the next morning after the intestinal lavage. Everything went well from June 8 to 16, when after an excellent night the little one was taken with a chill and the regular train of symptoms following. The fever was controlled as before with aconitine and veratrine, then the quinine pushed. It was associated with quinine arsenate and strychnine arsenate later in the treatment. This cured the case and the spleen was soon restored to normal size.

Other cases are reported which it is not necessary to study here in detail. The above shows the uniform success attained by Dr. Van Renterghem by this method. He is naturally enthusiastic as to the value of the associated use of quinine, arsenic, strychnine and hydrocyanic acid in the treatment of paludal disease, given after the small, repeated dose method.

Neuralgia Treated With Quinine Hydroferrocyanide.—In neuralgias this medicament renders singularly good service. It should be given during the paroxysm and should be associated (according to the nature of the symptoms present) with aconitine, strychnine arsenate, hyoscyamine, morphine, and caffeine; above all, give strychnine during the intervals in order to prevent a new attack.

Quinine Hydroferrocyanide in the Treatment of Phthisis.—At the meeting of the International Congress of Dosimetrie, in 1900, Dr. Lannoise advocated the use of quinine hydroferrocyanide in the treatment of tuberculous hemoptysis, and cited one case, which had lasted eight days in spite of all other medication, where the bleeding was rapidly arrested by the administration of three granules of this remedy every hour. The result in this case is probably explainable by Laura's teaching, that quinine hydroferrocyanide has a special influence upon the cardiovascular circulation.

Of its action in phthisis, two conditions are noteworthy: First, as suggested by Van Renterghem, it acts as a sedative in the first stage of phthisis; second, as pointed out by Lannoise, it has a hemostatic action.

As regards the latter point, Salivas gives additional evidence. He reports a case of bloody expectoration which had lasted for

three weeks and in which ergotin, hamamelis, chloral hydrate, perchloride of iron, injections of morphine, dry cupping, sinapisms, ice and absolute rest had all failed. Recalling Lannoise's communication on this point, he had recourse to quinine hydroferrocyanide, giving three to four centigrams every hour. In two days the blood had entirely disappeared from the sputa. After this the remedy was tried in four other cases of hemoptysis, equally refractory, and with equally satisfactory results.

Salivas also tried the remedy in the treatment of the evening fevers of phthisis, but here it proved disappointing. He was, however, able to demonstrate that it has a remarkable calming effect upon the cough of tuberculosis, thereby sustaining Van Renterghem's statement. A most striking example was found in the case of a girl, eight years old, both of whose lungs were involved, the left worse. The painful and nearly incessant cough, which was only slightly ameliorated by the use of codeine, nearly disappeared when quinine hydroferrocyanide was added to the codeine.

In addition to the effect upon cough and its checking of hemorrhage, quinine hydroferrocyanide is valuable in phthisis on account of its tonic and reconstituent properties. "And yet," says Salivas, "I have not seen many remarks by dosimetrists touching the employment of the remedy in that disease. This is to be regretted and it is very desirable that more frequent recourse be had to quinine hydroferrocyanide in a disease in which we have so few really helpful remedies."

Salivas adds the following remarks concerning the little girl just mentioned:

"The little patient became phthisical in consequence of scarlet fever which she had two years before. There was no history of family taint. I saw the patient first in February after she had been examined and condemned by five other physicians and she was really in a very serious condition. Her left lung presented a large cavity and mucous râles could be heard all over the right lung. Expectoration was very abundant and of a greenish color. She also complained of severe night-sweats and evening fever, which never missed coming about 3 p. m. and ended before 1 or 2 a. m., the temperature running to 104° F. Attempts had been made to control it with quinine and antipyrin, but without success.

"When I took charge of the case I replaced these remedies with the dosimetric trinity, which seemed to do some good, though not as much as I expected it would, though it was given for a number of days with all the precision and care of our school. To the trinity

I added quinine hydroferrocyanide, which was given for two weeks and while it did not act as a defervescent it ameliorated the cough very nicely.

"The quinine hydroferrocyanide was continued, together with the trinity and the fever stopped at last; and what proved the efficacy of the quinine salt was, that as soon as it was omitted the fever reappeared, and when it was restored and given with the dosimetric trinity it fell again."

In this case the remedy was taken in five to eight one-centigram granules (1-6 grain) a day.

Form and Dosage:—Quinine hydroferrocyanide may be administered in granules or in solution. The French granules are made in one-milligram doses (gr. 1-67). This dosage is excellent for infantile practice but Van Renterghem says that he would be glad to see them made in one-half to one centigram doses. The American granules are made in 1-67 and 1-6 grain doses, thus meeting this need.

Van Renterghem never saw the need of going beyond Gm. 0.15 to 0.3 (gr. 2 1-2 to 5) in one day, for adults, in intermittent fever. If the fever does not yield for these doses it is best to keep on with it but to associate with it quinine arsenate, iron arsenate, sodium arsenate, and, of course, strychnine arsenate.

In spite of the very pronounced bitterness of this remedy Van Renterghem always succeeded in administering it to very young infants. All we have to do is to crush the granules and dissolve them in a sufficient quantity of sugared water, or better still, in a watery solution of licorice.

Dr. W. T. Thackeray, of Illinois, says: "The writer's attention was first directed to quinine hydroferrocyanide in a rather peculiar manner. In the early eighties, while traveling in the counties bordering on the Mississippi south of Rock Island, I found the demand for quinine sulphate simply immense. Everybody was shaking, even the doctors.

"There was one exception: In a town south and east of Beardstown, the name of which I have forgotten, I met a Dr. Meacham; and as a matter of course the question of quinine sulphate as an antimalarial was discussed, and for the first time I heard its efficiency questioned in favor of, as the doctor called it, a prussiate of quinine. As I was at that time selling pills, Dr. Meacham inquired for a price on 100,000 pills, each to contain quinine alkaloid 1-16 gr. and Prussian blue 1-4 gr., with sufficient excipient to make a half-grain pill. Then, having some little time on my hands, through the

kindness of the doctor we visited several of his patients, who had been treated with his "little blue pills," as they were called by his neighbors. I found to my surprise a much-improved condition among those visited over those seen in the surrounding neighborhoods, which condition Dr. Meacham assured me was due entirely to his use of his prussiate of quinine pills, in the dose named, at frequent intervals, until therapeutic effect. And, he added, "There is no unpleasant after-effect, no quininism."

"A renewal of the thoughts suggested by Dr. Meacham came to me when first reading Dr. Burggraeve's "Manual of Dosimetry," and finding there the assertions that "above all, the quinine hydroferrocyanide was the remedy in malarial troubles," and that this was due to the fact that the antiperiodic properties of the quinine were largely increased by the peculiar action of the hydrocyanic acid, in the chemical combination which took place upon their mixture.

"My intimate connection with the practice of dosimetry or alkalometry, during the past eighteen years, has brought me in contact with many observers who have been and are using quinine hydroferrocyanide as an antiperiodic and antimalarial; and without a dissenting voice the clinical experience of Dr. Meacham has been confirmed. And while his pill was simply a crude mixture of two substances without chemical affinity for each other, the fact was established and the clinical experience confirmed by Burggraeve and others, of the positive effects of the quinine, iron and hydrocyanic acid in chemical combination.

"As the etiology of malaria was still in doubt, and as no positive malarial parasite had been identified, and as quinine hydroferrocyanide had not been proven to be a bactericide, its use, like many other valuable remedies, was empiric. But I most heartily endorse this empiricism, and recommend it to my confreres. Quinine hydroferrocyanide has been too much neglected by the profession. Try it, Brothers, and you will use it. 'Those who come to scoff, remain to pray.' "

E. T. Meacham had a severe case of malarial fever, the temperature reaching 105° F. He gave one dosimetric triad granule every half-hour till the fever abated, then less frequently; three granules of quinine arsenate and three of the hydroferrocyanide alternately every hour. The next day the patient was well and there was no return of the malady.

A. A. C. Williams reported a lady, ill one week, temperature 103° F., bilious, etc. The bowels were cleared by leptandrin and podophyllin, and the fever subdued by aconitine and digitalin,

a granule each every half-hour, with an occasional granule of hyoscyamine. By the fifth day the fever had fallen to 101° F., when she was placed upon quinine hydroferrocyanide two granules every two hours, and one granule of strychnine arsenate every three hours. Recovery within eleven days.

S. F. Meacham tells of a patient whose fourth chill was a pernicious one, for which he was given a hypodermic of morphine, with strychnine and hyoscyamine every fifteen minutes until reaction was established. The fever was controlled by the defervescent compound granules, given every fifteen minutes; and quinine hydroferrocyanide, gr. 1-6, every half-hour for six doses, then every hour. The bowels were emptied by saline laxative. There was a slight chill next day, but none thereafter.

The same writer tells of a child with chills, treated unsuccessfully for two weeks with quinine sulphate; lienteric diarrhea and anemia were present. Calomel was given for the vomiting, followed by salines, gelseminine for nervousness, and quinine hydroferrocyanide. But one solitary chill followed and the child recovered on pepsin and strychnine.

In a case of severe remittent fever, temperature 105.4° F., patient dreading quinine, he gave aconitine and veratrine every fifteen minutes till the fever had fallen to 103° F., then every hour; quinine hydroferrocyanide gr. 1-6 every hour. The patient was dismissed on the third day.

To a patient who had been suffering trifacial neuralgia for three days, he gave quinine hydroferrocyanide gr. 1-6 every half-hour for six doses, the fourth dose giving relief.

Quinine is not merely quinine, but the acid with which this base is combined may well be credited with a part of the effects. We have repeatedly called attention to the notable effect of the minute quantity of bromine to be found in the bromides of gold, arsenic, nickel, etc., and also to the great value of quinine arsenate as compared with the sulphate in treating malarias. The above reports indicate that the hydroferrocyanide of quinine may be far more effective than the sulphate, the acid aiding the base in its antiplasmodial action, so that better results are obtainable than from much larger doses of either element singly. This is too important to be neglected, if true, since the large dose of the ordinary quinine salts is the greatest objection to them.

The ferrocyanide is insoluble in water, and this renders it suitable for children as it prevents the bitterness developing as it is swallowed. This is the quality that made cinchonine famous

as "tasteless quinine." Quinine arsenate is only soluble in hot water; the bisulphate in ten parts of water, hydrobromide in 54, hydrochloride in 34, salicylate in 225, sulphate in 740; valerate in 100 parts.

The observers quoted fix the ordinary dosage of quinine hydroferrocyanide at gr. 1-6 every half-hour in pernicious and other severe forms of malaria. This dose appears to have sufficed even in these dangerous cases. The remedy is, however, safe, though of doubtful utility, in far greater doses, as Merck gives the dose as 5 to 10 grains. Possibly such a quantity administered at bedtime may be effective in preventing the development of asthmatic paroxysms, or the hectic and subsequent night-sweats of phthisis. To children the little granules containing gr. 1-67 may be given hourly.

Our own experience justifies every claim made for this valuable drug and we earnestly urge its trial.

RESORCIN

Standard granule—gr. 1-6, Gm. .01.

Resorcin is a synthetic product, one of the few that seems worthy of a place in modern therapeutics. It is soluble in water, alcohol, or glycerin. Injected subcutaneously it causes little inflammation and no suppuration. In doses of gr. 30 to 60 it acts as an antipyretic, reducing the temperature for some hours, but causing nausea and symptoms of marked depression. Larger doses are dangerous, and death has been caused in children by washing out the stomach with a 3-percent solution. It is excreted with the urine, and has caused hemoglobinuria.

The symptoms of overdoses call for stimulants and hot drinks, with atropine and strychnine hypodermically.

Resorcin is antipyretic in the doses named, but has been superseded by safer and not less efficient remedies of this class. It is antiseptic, but the sulphocarbolates replace it as well and more safely. It is antirheumatic, and in cases with evident gastric fermentation and high fever resorcin may be well suited, especially when the salicylates are not well borne. Here it is best to give the small dose, gr. 1-6, every five to thirty minutes, till improvement is decided. Resorcin is also astringent, and possibly in the declining stages of cholera infantum and other gastrointestinal maladies it may be appropriate; though the sulphocarbolate of zinc leaves little to be desired in this respect. In fermentative dyspepsia resorcin is useful, and may be given as recommended for rheumatism.

Locally resorcin has been extensively employed as an antiseptic and astringent, and with benefit. The applications are too numerous and too obvious to require enumeration.

RHEIN

Standard granule—gr. 1-6, Gm. .01.

Rhein is a concentration from rhubarb, the root of Rheum officinale.

Rhubarb contains a glucoside chrysophan, besides emodin, chrysophanic acid, phaeoretin, erythrorhetin, aporhetin, rheotannic and rheumic acids, and certain resins. Dragendorff attributed the purgative principle to the cathartic acid, while the astringent tonic action is due to the tannic acids, the antiseptic effect to chrysophanic acid and emodin. Hesse also obtained a crystallizable principle, rhein, but Tschirch attributes the purgative power to emodin, or chrysopan. However, the true values of rhubarb cannot be said to depend on any one of its constituents, as at present known, but upon their combination; and although forming an exception to the alkaloidal principle, we must content ourselves with the concentration until chemistry has advanced our knowledge. Yet it is one of the remedies that fills a valuable need, and cannot be replaced by any one of the modern remedies, though they have materially narrowed its field.

Therapeutics.—Rhubarb increases the saliva, gastric and intestinal juices and stimulates peristalsis; later its astringent principles exert their influence. This renders rhubarb especially suitable to the treatment of diarrheas where it is necessary to clear the gastrointestinal tract of offending matter and check the discharges later. In children especially this indication frequently presents itself. Rhubarb increases the secretion of bile, though not a powerful cholagog. In fact, it has the repute of stimulating the entire digestive system to secrete healthy, normal secretions instead of pathologic ones. The coloring matters are excreted through the kidneys and the renal excretion is increased. The purgative resins are excreted by the liver, intestinal glands, kidneys and skin. The nurse's milk contains enough to purge her nursling.

Rhubarb is used largely for the gastric and intestinal troubles of children due to improper diet, to cold, over-eating, and emotion. When the child is cross and fretful this remedy usually restores peace and happiness to the household.

It is also an effective remedy for colics dependent on undigested food or other irritating matter in the stomach or bowels. Travelers' diarrheas of adults or children from change of water, sea and car sickness, acidity with irritating discharges, and hemorrhoids, especially during or after pregnancy, are benefited by rhubarb. For gastric catarrh the best way to use it is to take one of the granules as a lozenge, dissolved in the mouth, every one to three hours.

In the early and mild forms of summer diarrhea and cholera infantum, rhubarb is most effective. Here it may be given with emetine, hydrastine and menthol, a granule of each every two hours till the stools passed are natural in appearance. Zinc or soda sulphocarbolate should be added if the stools are offensive. In cachectic, rickety children the sulphocarbolate of calcium with the above combination is excellent.

Felter and Lloyd give as the specific indications for rhubarb: Gastric irritation, nausea, vomiting, elongated tongue red at tip and edges; irritative diarrhea with soreness on pressure; sour smelling discharges imparting a sour odor to the child; gastrointestinal irritation with nervous irritability, restlessness, screaming and convulsive muscular contractions; constipation with a sense of intestinal constriction and abdominal contraction; light-colored fecal discharges.

Rhubarb seems unknown to the French dosimetrists, who have utilized juglandin largely as a substitute—and the writer has found the latter so satisfactory that he does not use rhubarb one-tenth as much as he did before he learned to use juglandin.

The dose of rhein for a child of two years is a granule every two hours till the stools are normal. For adults two to five granules may be given at the same intervals.

RHUS TOX.

Standard granule—M. 1-10.

The granules of rhus tox. are prepared from the green leaf tincture.

The effects of rhus are due to a neutral body, toxicodendrol, closely resembling cantharidin, anemonin and euphorbol (Pfaff). It is not volatile and the belief in poisoning from this plant without actual contact is said by Cushny to be without foundation. Toxicodendrol is a fixed oil, soluble in alcohol but not in water, rendered insoluble by lead Maisch claimed that the true active principle was toxicodendric acid, a volatile principle, and that the exhalations of vigorous leaves redden blue litmus, if previously dampened.

Felter and Lloyd say that rhus is a powerful local irritant, affecting persons with varying degrees of virulence, and that many persons are poisoned without actual contact, especially if the air is heavy and humid or the patient perspiring. Alcoholic solutions retain the virulence for years (Johnson). A lady in Lloyd's employ is not allowed in the building when rhus is being bottled, so intense are the symptoms produced by the emanations. The symptoms tend to recur monthly or yearly in some persons once poisoned by this plant. Horses, cows and sheep are unaffected by eating the leaves, but dogs and guinea pigs are killed by it. Drying or heating dissipates the toxic properties, at least in part.

The local effects consist of a dermatitis with itching and swelling, redness and sometimes vesicles, burning pain and fever. Sometimes pus forms. Headache and even delirium may be present in severe cases. The symptoms appear some hours after contact and the affection runs its course within a week. The skin desquamates.

Given internally, rhus acts on the kidneys and skin, slightly on the bowels. For paralyses it should be cautiously pushed until it causes prickling and burning, with twitching of the paralyzed parts, when improvement of sensation and motion will be manifest. Large doses cause vertigo, dilation of the pupils, impairment of the special senses, chilliness, nausea, thirst, burning in the stomach, temporal constriction, pulse slow, irregular and weak, urine and perspiration increase, weakness, trembling and faintness occur, sometimes convulsions, and a state of stupor or coma may supervene.

Felter and Lloyd vaunt rhus highly, saying its range of application is exceeded by few drugs. It is an ideal sedative, controlling the circulation and acting strongly on the nervous system. The specific indications are: The small, moderately quick, vibratile pulse, with sharp stroke, and burning sensations; nervous erethism; the sick infant sleeps disturbedly, frequently starting suddenly, with *cri encephalique*, often seen in cholera infantum and cerebrospinal meningitis. The circulatory disturbance requiring rhus is localized, in small cerebral or nerve centers. Restlessness is great in proportion. Frontal and left orbital pain, sharp; tongue red at tip and edges or strawberry with tympanites, brown sordes, red mucosa, acrid discharges, ichorous flow, disappearing by drainage. It relieves vomiting when with the tongue described. Great unrest with vomiting is a chief indication for rhus. Burning pain, deep or superficial, whether of the head, abdominal, thoracic or urinary organs, eyes or skin, is relieved by rhus quicker than by any other agent. It may be neuralgic, rheumatic, pleuritic, cystitic, etc. Rhus

cures burning and erysipelatous redness of the skin. It relieves rheumatic pain made worse by the warmth of the bed. It is better in acute than in chronic rheumatism, and in the articular stiffness following attacks. It controls the restlessness of rheumatics. It relieves toothache aggravated by heat. It is of value in bowel troubles of infants, diarrhea, typhoid dysentery, typhoid and malarial fevers with typhoid symptoms, and in cholera morbus. It is valuable in pneumonia, bronchitis, influenza and phthisis, when the patient is extremely irritable and the stomach irritated. With the small wiry pulse as a guide it controls restlessness and delirium in adynamic fevers; is indicated in typhoid pneumonias with red glazed tongue and fetid sputa; relieves dry tickling cough; and skin diseases with redness, swelling and burning. It is excellent for vivid bright red erysipelas, facial, with puffiness; acute dermatites; herpes with burning, itching and exudation; with iron in purpura hemorrhagica; vulvar erythema and erysipelas, with burning, and itching irritation following micturition; a special antizymotic in the exanthemata and all zymotic diseases; with vital depression, livid skin and foul discharges; red glistening swellings or edges of ulcers; parotitis, submaxillary swellings; carbuncle, furuncle; ocular swellings, to prevent inflammation after cataract operations, palpebral edema with redness, pains in the eye globe, acute or chronic conjunctivitis, catarrhal ophthalmia of scrofulous children with inflamed lids, photophobia, etc.; paraplegia without any organic lesion; paralysis of the bladder and rectum. But it is of little value in any paralyses save those following rheumatism. In sciatica it is efficient but concomitant rectal disease must not be neglected.

Specific Indications.—Small, moderately quick, sharp pulse, sometimes vibratile or wiry; great restlessness; with vomiting; tongue red and irritable, red spots, strawberry tip; burning pain; pain in or above left orbit; pinched face; burning urethral pain with dribbling, etc.

Ellingwood recommends rhus in acute rheumatism, with aconitie for fever, cimicifuga for deep-seated muscular soreness; in dry tickling bronchial coughs, with bryonia or aconite in capillary bronchitis; gastric or intestinal disorders of children with great restlessness and flushed face; and the specific tongue, mouth and mucous indications; prevents spasms from cerebral engorgement or reflex, or from gastric or intestinal irritation. He finds it most prompt and valuable in pruritus vulvæ with erythema, redness, especially in blonde children with eczematous or scrofulous tendencies.

Dr. R. E. Buchanan reports excellent results from rhus in lumbago, acute muscular soreness, torticollis, and similar myalgic troubles.

Dr. John Aulde is one of the few who have studied this remedy. He finds the first effects of remedial doses to be stimulant to the cerebral functions, differing with the great disparity in its effects in various individuals. The effects upon the skin are due to the endeavor of the epidermic cells to drive out the intruder. This renders this agent suitable in affections showing sluggish skin-action, or inactivity of the cellular structures. He recommends rhus in scaly skin diseases, subacute and chronic rheumatism, and as a quick means of relieving the pain of rheumatic gout.

Dr. A. T. Cuzner testifies to the efficiency of rhus in rheumatism.

Dr. C. W. Smiley writes that while suffering from nervous debility and general prostration, insomnia and great irritability, he was attacked by rhus poisoning after free exposure to the weed. Soon after he found his health had undergone a remarkable change for the better, and he was soon boasting of complete recovery. He attributes the result to the free elimination of toxins, caused by the rhus.

Rhus is very effective for the leaky bladder of women; a granule three to seven times a day.

Dr. J. M. Blackerby found rhus successful in sciatica; facial erysipelas; synovitis of both knees, subinflammatory, tongue red and pointed, bowels acting naturally, urine scanty, red and offensive, pulse 108, temperature 101.5, heart feeble—patient a man aged 22.

In *The Alkaloidal Clinic* some years ago the subject of rhus poisoning was discussed at length, and many physicians suggested remedies for it. Of these the local application of sweet spirit of niter seemed to have the most decided and prompt effect in relieving the symptoms and curing the malady. Webster reports one patient treated by echinacea locally and internally, who was not only cured but henceforth proved immune against the poison. Among other remedies named were alnus, apocynin, hydrogen peroxide, pilocarpine hypodermic, sodium bicarbonate locally, aristol, lobelia locally, lead and laudanum, white oak bark infusion, quinine ointment one to 8, sodium bisulphite 5-percent solution with one percent of carbolic acid, dilute alcohol saturated with lead acetate and well rubbed into the skin, zinc sulphate one to 15 of water, hamamelis, serpentaria, sodium hyposulphite saturated solution, and numerous others.

Some persons appear to be immune against the effects of rhus, and they are said to be also immune against its remedial operation. The more susceptible the patient, the more certain is rhus to cure his maladies when correctly prescribed.

In administering rhus it is best to give the granules containing but a fraction of a drop, and repeat them every half-hour until tangible effects are manifest. This avoids the painful rhus toxication in persons unusually liable to it, and ensures action in those difficult to affect by it.

RUMICIN

Standard granule—gr. 1-6, Gm. .01.

Rumicin is a concentration from Rumex crispus, the yellow dock.

Rumex contains chrysophanic and oxalic acids.

Felter and Lloyd pronounce rumex decidedly alterative, tonic, mildly astringent and detergent. They recommend it in scorbutic, cutaneous, scrofulous, scirrhous and syphilitic affections, leprosy and elephantiasis; finding the plant inducing retrograde metamorphosis, increasing innervation and improving nutrition; in bad blood with skin disorders, chronic lymphatic enlargements, with tendency to indolent ulcerations and low inflammatory deposits; small doses in nervous dyspepsia with epigastric fulness and pain, aching or darting pain in the left chest, gastric flatulence and eructations; for painless watery diarrhea; cough with fulness of chest, sighing, yawning, efforts for full inspiration; best in lung ails with bad blood; respiratory catarrhs and sore throat with hypersecretion, and even in incipient phthisis; dry stubborn summer coughs (Webster); internally for contagious prurigo.

Specific Indications.—Bad blood with chronic skin diseases; bubonic swellings; low deposits in glands and cellular tissues, tendency to indolent ulceration; feeble recuperative power; irritative, dry laryngotracheal cough; stubborn, dry summer cough; chronic sore throat with enlarged glands and hypersecretion; nervous dyspepsia with epigastric fulness and left thorax pain; cough with dyspnea and precordial fulness.

Ellingwood values rumex as a renal depurant and agent to remove morbific matters from the body; for ulcerative stomatitis, nursing sore mouth, gastric ulcer with atony, it has no equal. It has cured obstinate morning diarrheas.

Rumicin seems to be best administered in doses of one to six granules for an adult, before meals and at bedtime. Give for

several weeks or longer—it is not a remedy for immediate effect. It would be a good adjuvant to arsenic iodide.

SALICIN. SALICYLIC ACID

Standard granule—gr. 1-6, Gm. .01.

Salicin is a glucoside from Salix nigra, found in many species of willow and poplar. It is decomposed and oxidized into salicylic acid in the alimentary canal, and exerts the effects of this acid in the body. It is excreted through the urine. Salicin is less irritant to the stomach than the acid.

Salicylic acid and its congeners are as antiseptic as carbolic acid but far less toxic. The salicylates are also much less irritant than the acid. It retards digestion, affecting every one of the ferments injuriously. It also retards the putrefaction of proteids and the alcoholic and acetous ferments. Its effects in this respect are less powerful than those of carbolic acid but last longer. The motion of protoplasm, protozoa and leucocytes is prevented by the acid.

Salicylic acid and its salts are quickly absorbed, and give rise to unpleasant symptoms only when given in large doses. They cause a sense of heaviness and fulness in the head, roaring in the ears like that of quinine, followed by confusion and dulness, with disorder of sight. Free sweating and a sense of heat may occur. Dyspnea has been noted, with evidences of collapse. The pulse is weak, the temperature subnormal, and partial or complete unconsciousness may follow. In some cases delirium, hallucinations of sight and hearing, have been noted, especially in alcoholics and diabetics. Albuminuria and hemoglobinuria have also occurred. Skin eruptions are more common from its long continued use than from too large doses. Abortion occurs sufficiently often to render pregnancy a contraindication. Hemorrhages may appear, especially from the nose.

But to all the foregoing there is to be added the following: Hare collected a large number of cases of poisoning by these agents, showing that in some so small a dose as 15 grains caused toxic symptoms, while in others two ounces were swallowed without causing death. It seems quite certain that the commercial synthetic acid and its salts are contaminated by impurities to which most of the toxic symptoms are really due; while the chemically pure acid and its salts do not irritate the stomach or depress the heart in any doses likely to be given medicinally.

The affections of hearing are due to congestion, even extending to inflammation; they rarely leave permanent diminution of hearing; the dimness or loss of sight is due to vascular constriction possibly; the cutaneous vessels are dilated, the pressure increased by small doses, lowered by large ones; small doses accelerate the heart, large ones slow it, from direct action on the heart; the respiration is faster from central action, the center being depressed and paralyzed later, from which death ensues.

The effect on the central nervous system is slight. Sweating is due to dilation of the cutaneous vessels, which may explain the rashes. The urine is increased, as is the production of urea, the bile solids but not the fluid. The normal temperature is only lowered by toxic doses. Fever heat it often lowers. The fall is due to dilation of the skin vessels and to an increased radiation; it is less and of shorter duration than the fall caused by antipyrin.

Salicylic acid modifies metabolism, increasing the nitrogen and sulphur eliminated by the kidneys by over 10 percent. The excretion of uric acid is increased from 30 to 100 percent. The leucocytes increase in number. Mainly excreted in the urine, salicylic acid is found in the milk, perspiration and bile, but not in the gastric juice.

The use of this acid as a preservative of foods and beverages is now forbidden by the laws of many countries. The effects upon the digestive ferments justify such legislation; and besides the use of such preservatives enables the unscrupulous packer to dispose of products in which decomposition has already progressed beyond the point of wholesomeness.

Van den Corput states that salicylic acid lessens the functional activity of the testes, and Salix nigra has long had the reputation of suspending the sexual powers. Yet the same agent is believed to congest the uterus and ovaries.

Sollmann says that the effects of salicylic acid differ from those of phenol by the smaller centric action, the almost complete absence of convulsant effect, less tendency to collapse, and greater antipyretic power. There is less local irritation. The salicylates increase the flow of bile, and are slightly diuretic, increasing the excretion of uric acid markedly, by the destruction of proteids; the sulphate and nitrogen excretion is also raised. An hour after taking salicylates the number of leucocytes is doubled, but within two hours it has become normal. Excretion of the acid is completed in twenty-five hours. Mendel gave sodium salicylate intravenously, in solution with caffeine.

Therapeutics.—Salicylic acid and its salts and derivatives have all been used with benefit in rheumatism. The greater the pain and higher the fever, the more prompt and powerful is the beneficial action of this remedy. Hence it is better in young subjects than in the middle aged or elderly. It is best given to rheumatics in doses of 1-6 grain, repeated every ten minutes till the ears begin to ring. This gives better results than bulky doses that may irritate the stomach. As a preventive of cardiac affections it does not equal the alkaline treatment. The salicylates of iron and quinine may be employed in suitable cases.

We assume that rheumatism is due to the formation of toxins in the stomach and duodenum, since every remedy that has won favor for this malady is an antiseptic—salicylic acid, resorcin, quinine, etc. Very small quantities of salicylic acid suffice to prevent this fermentation, and very large doses are wasted. I have administered this acid in doses of gr. 1-6 every ten minutes, in acute rheumatic attacks, and secured better results in this way from a grain an hour than from thirty grains every four hours. This provides for a trace of the acid always present in the affected region, and a trace suffices to prevent fermentation.

Burggraeve found salicylic acid useful in all zymotic affections to combat putridity and ataxy, especially in gangrene and typhus. Even in moderate doses it may occasion grave troubles of the circulation, especially in the vasomotor functions of sensation and motion, and in the cerebral functions, in disquiet, mydriasis, strabismus, cephalalgia, albuminuria, gangrenous ulcers, hallucinations and delirium. These phenomena increase with excessive doses (Laura). Lepert employed it to lower temperature in miasmatic affections, typhoid and scarlet fevers, and to modify the morbidity of the urine in pyelitis and cystitis. Chirone and Petrucci found that this acid invariably lowered temperature and caused emaciation, lessening the number of the heartbeats and the respirations. It is eliminated by the kidneys. Lussana and Ciotto injected it under the skin and recovered the free acid from the ventricle. Laura did not find the defervescent action as invariable as that secured from the defervescent alkaloids. Wagner employed salicylic acid as an antiseptic in diphtheria. I have often applied it with marked benefit for the angina of scarlet fever, and believe it specifically useful in preventing the dangerous development of this local malady. Kolbe and Paulcke employed it locally for fetid sweating of the feet, and it forms the active ingredient of the powder used for the feet of German soldiers. In small doses Danowscki

found it strengthened the heart, respiration and vascular pressure; larger doses reversing both actions.

Moore found that in doses of fifty centigrams a day salicylic acid interfered with the development of vaccination. Laura limits its application in rheumatism to the acuter manifestations, rheumatic iritis, even muscular forms; but it is better to meet fever with the alkaloids at the same time and to depend on the salicylic acid to stop gastric fermentation. Laudon praised it in malignant scarlet fever. In diphtheria Ruatta's results were equivocal. Laura found calx sulphurata preferable. Salicylic acid seems to have some effect in saccharine diabetes, when combined with arsenic and a rigid diet. It is very useful in catarrhal dyspepsias, especially of infants, but not so applicable as the sulphocarbolates. Laura advises that its administration should be suspended whenever the face reddens, without waiting for cerebral symptoms. If the symptoms persist, watch carefully the heart and the pulse, guides always precious, remembering that any medicament that affects the circulatory centers badly either does not suit the case or is being improperly applied.

Acute forms of myalgia, such as lumbago, torticollis, pleurodynia, and the numerous forms of abdominal and dorsal myalgia, are quite satisfactorily relieved by this agent. Gout and rheumatoid arthritis are also relieved by an agent that stops fermentation in the alimentary tract; but the writer has never obtained the slightest benefit from it or any form of salicyl in gonorrheal rheumatism.

Chronic forms of the above affections are only benefited by salicyl as it checks acid fermentation. Many maladies may be traced to this source, neuralgias, neuroses, skin diseases, iritis, and tonsillitis. Gay gave the acid successfully for Meniere's disease, in doses of gr. 10 daily. Strizower recommended it for gallstones, gr. 10 four times a day. Shoemaker gives it for worms, gr. 8 hourly for five doses; and for the foul breath of phthisis. Monin employs it for diabetes.

As an antiseptic antipyretic this acid has been given in typhoid fever, pneumonia, erysipelas and phthisis, and especially in blood-poisoning, pyemia, sapremia, etc. De Rosa claimed it was prophylactic against scarlet fever. Dr. C. A. Bryce, of Richmond, Va., finds that in smallpox it reduces fever, relieves pain and limits the development of the pustules.

Salicylic acid quickly checks the development of sarcinæ ventriculi.

As an analgesic salicylic acid in doses of gr. x has relieved the pangs of cancer. Bernheim injected it into inoperable cancers of the cervix uteri in five cases, with decided benefit. His solution was made with 90 grains of the acid in an ounce of distilled water, adding 3 drams of glycerin and 4 drams of alcohol; of this he injected 30 minims into the substance of the tumor for five successive evenings.

Shoemaker recommends salicin as a useful bitter tonic in feeble digestion; for the diarrhea of phthisis, and for chronic diarrhea of children. Maclagan preferred it to the acid in rheumatism, as less depressing; also in neuralgias and coryzas. Turner used it in 200 cases of influenza with great benefit. Cheron advised it in pelvic pains of rheumatic origin, in metritis, cellulitis and peritonitis.

Salicin is Crocker's favorite drug in the treatment of psoriasis. He states that this drug is applicable to a wider range and is successful in a larger number of cases than any other remedy. He does not claim that it cures all cases, or that it cures every attack in any one patient, though it does in the majority; neither does he claim that it has any preventive action any more than arsenic has. But he does claim that in a large proportion of cases it is useful and that in a very fair proportion it is extremely successful. In a few it is rapidly successful.

The more acute and widespread the disease, the more salicin and its congeners are likely to be successful. In one case the treatment has been successful in each attack. But where there are chronic, hard patches, this remedy seems to have only a moderate effect. The indurated, thickened patches must have local treatment to remove the crusts. Without anticipating any striking improvement in them, there is a certain amount of benefit observable.

In order to get good results from salicin it is necessary to give it in fairly full doses. Begin with 15 grains three times a day directly after meals, and increase it up to 20 grains, and even up to a higher dosage. Salicin is soluble up to 19 grains to the ounce; therefore, if it is given in greater strength than that it must be suspended in tragacanth or some similar mucilaginous mixture [or may be given in powders or tablets].

The author gives salicin instead of salicylate of sodium because salicin seldom upsets the patient, as sodium salicylate often does. Salicin also can produce a rash of its own—an erythematous eruption of a transitory character; but since the writer has given it so

largely—in hundreds of cases—he finds the salicin eruption extremely rare, say not in more than one percent of the cases. If there is such a rash, it is generally morbilliform without itching, and disappears within a short period of the cessation of the drug. Sodium salicylate produces a good deal of depression in full doses, and he chiefly gives it when he has reason to believe there is hepatic indolence and stomach trouble, for which it often is useful; and he gives it more for its effects upon the gastrointestinal canal and liver than for its effects in psoriasis, although as an adjuvant it is often beneficial in both.

Cushny says that salicylic acid promotes the absorption of serous effusions, pleural and subretinal, in some unknown way.

Van Renterghem advises the salicylate of ammonia in fetid dyspepsia, pulmonary gangrene, typhoid fever, dysentery, and in flatulence; this salt decomposing in the digestive tube acts by both acid and base. Fuerbringer found that the acid was powerless in septicemia and pyemia. Bartels showed that persons saturated with the acid did not escape typhoid or erysipelatous infection.

Van Renterghem recommends salicylate of lithia for ammoniacal urine.

Salicin was once recommended for ague but proved less effective than quinine. Many persons cannot take the ordinary salicyl preparations but find among the numerous modifications on the market others which fully afford the benefits without the disadvantages.

The elimination of sodium salicylate by the kidneys commences within thirty minutes. It should be forbidden in grave disease of these organs. Mueller pronounced its action in diabetes useful but evanescent. Byasson observed uremia and Gubler albuminuria following its use.

Quinine salicylate is well defined, and agrees well with the stomach. It is a useful antiperiodic, in fevers presenting a rheumatismal element, or in those in which gastric fermentation is also present.

Iron salicylate suits the period of convalescence when there is fermentation, and when the fever persists when anemia is decided. Late in rheumatisms it finds a place.

Antimony salicylate was introduced by Lamy in 1885. He sought to combine the antizymotic action of the acid with the antifluxionary power of the base, taking for a point of departure the parasitic theory of rheumatism. We must not forget the powerful action of this as of all antimonials upon the stomach and bowels,

which renders them contraindicated in cholera epidemics (Laura). Lamy's conclusions were marred by his conjoint use of other powerful and effective antirheumatics with this one. In chronic rheumatism he preferred this salt to colchicine. While there may be presented forms of this malady in which excessive cerebral implication, in a young and plethoric subject, with furious delirium, might indicate the advantage of this combination, we would prefer to employ the salicylic acid by itself and give the ordinary forms of antimony separately, that the latter might be promptly discontinued when the brief need for it has passed. Laura's objections are well taken—to sanction a new remedy it should be tested alone.

The dose of salicin as a tonic is a grain before each meal. It is soluble in water and in alcohol.

In gastric fermentation quinine salicylate, gr. 1-6 every half to one hour, is quite effective.

SANGUINARINE

Standard granule—gr. 1-67, Gm. .001.

Sanguinarine is an alkaloid from bloodroot, Sanguinaria Canadensis. It has also been found in Chelidonium majus, and in Eschscholtzia Californica. Sanguinaria also contains chelerythrine, protopine and gamma-homochelidonine. The only form in which sanguinarine is used in medicine is the nitrate.

Small doses of sanguinarine increase the appetite and the digestion, strengthen the heart and slow the pulse, and excite the respiratory secretion. Larger doses cause a sense of warmth in the stomach, nausea, sedate the heart and slow the pulse, increase the perspiration, expectoration, urine, bile, and the menstrual discharge. Still larger doses cause violent vomiting, even catharsis, vertigo, troubled vision and great prostration. The saliva is increased. Violent gastrointestinal irritation ensues, with burning pain, relaxation, and the symptoms of collapse, cold clammy skin, dilated pupils, great thirst and anxiety, the spinal reflexes depressed, and death from paralysis of the respiratory and cardiac centers.

Sanguinarine is employed by the eclectics as an emetic, in conjunction with lobelia, in various febrile complaints when it is desired to thoroughly cleanse the stomach and arouse to activity the liver and digestive glands in general. Acting gently on the liver it is used in chronic hepatitis; in small doses for atonic dyspepsia, gastric and duodenal catarrh and jaundice; for sick headaches with torpid liver; for rheumatism, dysentery and scrofula with bad

circulation; for anemic amenorrhea and the dysmenorrhea of debility, with chilliness and headache; hysteria; hemoptysis vicarious in character; genital debility of men; syphilides, tinea, hypertrophic rhinitis (Felter and Lloyd).

The most important field for sanguinarine is in pulmonary affections. It is a stimulant expectorant, and especially indicated in the very aged or very young, when the sensibility of the respiratory mucosa is low and the patient does not feel the need of coughing to rid the tract of accumulating secretions. In this particular condition sanguinarine has no equal. It arouses the sensibility and makes the patient cough harder until the secretion is ejected and the danger past. Great care must be taken not to exceed the stimulant dose and get the sedation and nausea of overdoses. The indication for this remedy may arise in pneumonia, bronchitis, phthisis, and especially in capillary bronchitis.

Another indication for sanguinarine is found in acute respiratory catarrhs. The existence of disease in these tissues predicates a condition of low vitality there—else the tissues would have been able to resist the attack of disease-producing agencies and throw off the malady. Hence the indication for a special inciter of the vitality of these tissues, such as we find in sanguinarine. How far this principle of therapeutics can be carried is uncertain. In acute pharyngitis the application of a strong mixture of hydrochloric acid, potassium chlorate and tincture of iron, in which free chlorine is present, has frequently aborted the attack when applied early. The action may have been antiseptic, stimulant, vital incitant, or simply astringent—and we incline to the latter view. If sanguinarine exerts the influence suggested, it does so when given in dose strictly physiologic, that is just short of those arousing notable symptoms. It is a pity the varying effects of different doses are not better studied.

Felter and Lloyd further recommend this agent in acute and chronic nasal catarrh, humid asthma, whooping-cough, membranous croup, and scarlatinal sore throat.

Specific Indications.—Tickling or irritation of the throat, with cough, burning or irritation in fauces, larynx, pharynx or nose, with red surface and thin, acrid, burning or smarting discharge, dryness of nasopharynx or throat and sharp lancinating pain, and a feeling as if the walls of the throat rubbed against each other; poststernal constriction, uneasiness at the suprasternal notch with difficulty in breathing; uneasiness and burning in the stomach with nervousness.

The dose of sanguinarine nitrate as a stimulant expectorant is gr. 1-67 to 1-22 every hour till effect, relief or slight nausea. For anemic amenorrhea give gr. 1-22 to 1-12 before meals and at bedtime, during the intermenstrual period, with iron arsenate; adding apiol during the menstrual week.

SANTONIN

Standard granule—gr. 1-6, Gm. .01.

Santonin is a glucoside from German wormseed, Artemisia maritima.

It is very insoluble in water but rendered soluble by alkalies with which it unites to form santonates. It is slightly soluble in the stomach but most of it passes into the small intestine where it exerts its influence. Some of it is absorbed into the circulation, causing a peculiar disorder of vision, things appearing to the patient of a yellowish green. The urine assumes the same color. If very large doses are taken the darker colors become invisible, blue seems green, and visual hallucinations may occur. The senses of taste, smell, and rarely, that of hearing, may be deranged. Very large doses cause twitching of the head muscles, rolling of the eyes, grinding the teeth, followed by epileptiform convulsions; with contractions of the muscles during the intervals. Death during the convulsions is due to asphyxia. Confusion, or aphasia, nausea and vomiting may occur from ordinary doses. The convulsions are attributed to stimulation of the cerebral cortex, the interval contractions to increased activity of the parts lying between the cerebral peduncles and the medulla (Cushny). Large doses also affect the cord. Santonin lowers the temperature in most animals (Harnack). It is partly oxidized in the tissues and is excreted in the urine and feces in several forms. Two days are required for the elimination of an ordinary dose. The quantity of urine and frequency of micturition are increased. Urticaria has appeared after its prolonged administration, and even from one three-grain dose.

Therapeutics.—Santonin is the standard remedy for round worms. Solutions do not kill these worms outside of the body, and its remedial action is obscure. Von Schroeder suggests that it renders the intestine an unpleasant abiding place for them—which is a very poor explanation. Precise observations made in a London hospital showed that santonin did not entirely remove the parasites, since their eggs continued to appear in the stools after full treatment with it. Against thread- and tapeworms santonin is useless.

The dose of santonin for a child three years old is a grain three times a day. It is usual to combine small doses of calomel—gr. 1-4—with it. Lewin advises giving santonin in castor oil to hinder absorption from the stomach, but quite recently a French writer asserted that, in combination with castor oil, santonin appears to produce some of the poisonous symptoms observed with oleoresin of aspidium and castor oil, causing complete prostration and blindness.

The same writer says that the drug should not be given to children under two years of age and for older children he counsels only doses of 1-3 to 1-4 of a grain.

Empty the bowels first by suitable laxatives, then give the day's dose of santonin, and follow in four hours with a smart laxative. Otherwise the worms may be digested and the efficacy of the treatment be uncertain.

In poisoning by santonin, empty the stomach and bowels promptly, control the convulsions by chloroform or chloral, and sustain the powers as failure threatens.

The notable effect of santonin on the nerve centers has led to its employment in other maladies. Lydston gives it for epilepsy, instead of the bromides. It is a good antispasmodic for children, says Shoemaker; but we are well supplied with approved agents in this respect. Lydston begins with doses of gr. 2—5, for adults, and pushes it to tolerance. Saturation is denoted by the yellow urine, xanthopsia and vesical irritability.

Negro found santonin relieve the painful crises of ataxia; giving it up to gr. 22 daily.

Santonin has been given for color blindness, with some benefit in noncongenital cases. In other ocular maladies it has not succeeded. Nocturnal enuresis sometimes yields to it (Shoemaker). In anemic amenorrhea Whitehead gave santonin gr. 10 at bedtime repeated once, with benefit; and Masterman found this remedy relieved uterine colic dependent on suppression of the menses.

SCILLITIN

Standard granule—gr. 1-67, Gm. .001.

Scillitin is a glucoside from squill, Scilla maritima.

From squill Merck obtained three principles, scillipicrin, scillitoxin and scillin. Von Jarmerstedt and Kurtz obtained scillain, an amorphous bitter principle, soluble in water or in alcohol.

Vogel describes scillitin as a solid diaphanous mass, colorless, of resinous fracture, pulverizable, at first bitter, then sweetish, very hygroscopic, easily soluble in water, rectified spirit or acetic acid.

Tilloy separated from this body a purer scillitin and a non-crystallizable sugar. This body does not dissolve readily in water but is freely soluble in alcohol. Landerer and Marais believed they had discovered an alkaloid, scillitine, which is probably Merck's scillitoxin. Jarmerstedt's scillain is pronounced by Van Renterghem a pure scillitoxin. Of this a dose of 1-10 milligram kills a frog, 2 milligrams a cat. It shows close analogies with digitalin.

Fronmueller pronounced scillipicrin a diuretic which had no superior. Out of 17 cases of grave oliguria treated with it 15 were successful. It was not found suitable for hypodermic use, the irritation caused by it being too great.

Von Schroff found the action of scillitin bearing upon the ganglionic nervous system and the secretory organs, especially the kidneys and the respiratory mucosa. In massive doses it occasioned nephritis and gastroenteritis, with parenchymatous pulmonary hemorrhages. Lethal doses killed by ganglionic paralysis, especially of the heart. He classed this body with colchicine and helleborein.

Gubler found scillitin toxic in doses of gr. 5-6, smaller doses causing acute gastroenteritis. It acted as a violent emetocathartic. Narcotism followed, and death from heart paralysis. Applied hypodermically it acted quicker, and the effects were almost purely narcotic. Koenig after long experimentation on animals obtained no toxic phenomena.

Huesemann concluded that squill in medicinal doses causes slowing of the pulse with a rise in arterial tension; lasting some hours; light laxative action with liquid stools; long-continued use disordered the digestion; no narcotic phenomena were noticed. Excessive doses caused nausea, vomiting, diarrhea, slowed the pulse to 40, with prostration, narcosis and convulsions. One dose of 22 1-2 grains of squill killed a man. Toxic doses suppress the diuresis and cause hematuria.

In medicinal doses squill reduces the frequency of the heart action and increases its forces, as well as the vascular pressure, increases the excretion of urine, and of the respiratory mucus. Toxic doses cause gastrointestinal inflammation, and kill by paralyzing the heart. The active principle which most closely represents the plant is scillain (Van Renterghem).

Therapeutics.—Scillitin may be employed as a substitute for digitalin, over which it has the advantage of not being cumulative. It should not be given in congestive conditions of the kidneys, stomach or bowels.

Laura says that while scillitin does not represent all the properties or energies of squill, it is its medicamentous, expectorant and diuretic principle. Its action on the heart resembles that of digitalin. The former is more diuretic in small doses, but large doses diminish the urinary secretion. Burggraeve recommended it in humid asthma. It is of service in cases of bronchial catarrh with feeble and difficult excretion, the sputa being crude and glutinous. It is especially useful in capillary bronchitis, and in cardiac dropsies. With digitalin and calomel this combination has proved more effective than either agent separately. Give scillitin gr. 1-67, digitalin gr. 1-67, and calomel gr. 1-6, together, every two hours till the result is satisfactory. In advanced cardiac dropsies when other diuretics have lost their effects this combination will frequently prove surprisingly effective. But the principles of treatment of this malady comprise something far beyond the simple abstraction of a few ounces of serum from the body. If dry diet and elimination are not insisted upon, the results of any treatment will be but transitory.

Scillitin resembles sanguinarine in its power of increasing the sensibility of the respiratory mucosa, and making the patient cough harder. This and a slight increase of the mucous secretion comprise its effects in respiratory affections, and the combination of squill with sedatives like paregoric is one of the curious instances of incompatible mixtures common in the old polypharmacy. No case can be imagined that requires the two at the same time.

The dose of scillitin is gr. 1-67 every hour or two; or five granules every four hours, as a maximum.

SCOPOLAMINE

While hyoscine occurs as an uncrystallizable liquid, from belladonna or hyoscyamus, scopolamine from scopola was obtained by Benger in 1889 in the form of crystals. The differences between the physiologic action of hyoscine and that of scopolamine are accounted for by Hesse, who found in commercial scopolamine hydrobromide an admixture of a small proportion of atroscine, formula $C_{17}H_{21}O_4$, a base isomeric with hyoscine. Atroscine is a strong base which completely neutralizes mineral acids, and

ammonia. Alkalies liberate it from the solution of its salts in the form of oil drops.

Hesse made several salts, all soluble in water and crystallizing from it readily. As hyoscine and atroscine yield the same product on hydrolysis, it occurred to Hesse that it might be possible to convert hyoscine into atroscine. He had previously noted that hyoscine in alcoholic solution loses its activity when other alkalies are added to it, which led him to believe the conversion of the one into the other possible.

Schmidt has also obtained a well crystallized base from inactive scopolamine by the action of silver oxide, melting at 55° to 56° C., which he called i-scopolamine, i. e., indifferent scopolamine. Numerous experiments, however, convinced Hesse that the loss of optical activity was due to the conversion of the hyoscine into atroscine and scoparic acid, and that in no case was any other alkaloid formed.

The i-scopolamine is identical with atroscine. Scopolamine is therefore merely a mixture of hyoscine hydrobromide and atroscine hydrobromide, and not a chemical compound.

The above is taken from Shoemaker's "Therapeutics," quoted from a paper in the *Druggist's Circular*, October, 1896. The American Dispensatory and other therapeutic authorities are practically unanimous in the declaration that hyoscine and scopolamine are identical, chemically, physiologically and therapeutically.

Some years ago a similar identity was claimed for scopola root and belladonna, and the former was being employed extensively instead of belladonna, for the preparation of "belladonna" plaster. Clinical experience, however, showed a decided difference in their action, since the plasters made from scopola failed to surrender their alkaloids through absorption, as the true belladonna had done, and the Pharmacopeia now forbids such substitution.

Commercially, it is easy to see why the manufacturing chemist should desire to abolish the distinction, since he is now fully authorized to sell scopolamine under the name of and at the price of true hyoscine, although the latter still is quoted at a much higher price.

Clinical evidence is still wanting to determine conclusively whether there is any difference in the physiologic action and the therapeutic effect of these two drugs. As long as the body of the medical profession has not learned to distinguish between the applications of hyoscine and those of atropine, we cannot look for definite information on the much more difficult question of the identity and the non-identity of scopolamine and hyoscine.

So far as the chemical identity of the two is concerned, we leave it to the chemist to tell us how hyoscine, which is non-crystallizable, can be chemically identical with scopolamine, which crystallizes; and if this is due to the presence of atroscine in scopolamine and not in hyoscine, how about the chemical identity of the two!

Under the circumstances we feel that the only straightforward course is that true hyoscine from hyoscyamus shall be furnished to the profession under that title, and that scopolamine from scopola shall also be furnished under its own title. As there is material difference in the price of these two, the physician should have the privilege of purchasing the cheaper if he chooses. He should have the privilege of trying the two products and determining for himself whether their therapeutic applications are identical. If he finds there is a difference, and is willing to pay a larger price for hyoscine, he should have the privilege to do so. But under no circumstances should scopolamine be sold under the title of hyoscine and at the price of the latter.

Owing to the investigation by Lewin and Guillery, who saw unpleasant by-phenomena after the administration of scopolamine, Kobert attempted to find out whether or not some admixtures of other alkaloids in the commercial scopolamine or splittings of them, are to be blamed for those unpleasant side-effects.

He relied above all on the labors of E. Schmidt and Gadamer, who demonstrated that scopolamine occurs in two forms, viz., levorotatory (active) and the inactive kind, which Hesse, curiously enough, denominated with the special name "atroscine." Schmidt and Gadamer have shown that an alcoholic solution of active levorotatory scopolamine is turned into inactive scopolamine (they call it "atroscine, Hesse"), by the addition of but a few drops of caustic soda solution. Hence it will be almost impossible to demonstrate experimentally the preexistence of this inactive base in the Solanaceæ because the use of alkalies is unavoidable in the demonstration of the bases of the Solanaceæ.

Schmidt gives the melting point of genuine active scopolamine hydrobromide as 193° C. (375.4° F.) and for the "feebly turning," hence contaminated with inactive scopolamine, the melting point from 180° to 181° C. (356° F. to 357.8° F.). But the Arznei Buch, IV., demands a melting point of 180° C. and so causes the use not of the genuine active scopolamine, but one contaminated with the inactive base (atroscine, Hesse). But according to Kobert's investigation no inconvenience arises from this contamination with the inactive base (atroscine, Hesse), since it behaves itself quite

similarly to the active base. This is contrary to E. Merck's Index and other authors. Or does it produce the unpleasant secondary effects mentioned by Lewin and Guillery? On the other hand a preparation received from the factory of Riedel (Berlin), and designated as inactive scopolamine produced extremely unpleasant effects, manifesting themselves by eczematous formations and swelling of the eyelids. Examinations by Kobert and E. Schmidt showed that the trouble here arose from apoatropine, since this product had a higher melting point (232° to 233° C = .449.6° to 451.4° F.) than scopolamine hydrobromide, and derivatives from it with the corresponding derivatives of apoatropine showed equal physical and chemical constants (numerical values which are not subject to variations).

An experiment made at the same time with chrysatropic acid to see whether contamination with it might produce those unpleasant by-effects showed the physiologic inactivity of this substance. From these experiments it results that there is no guarantee for the purity of scopolamine from the melting point and the water contents alone, and that the Pharmacopeia must demand an active scopolamine for medical purposes which does not turn optically less than the genuine active scopolamine, according to E. Schmidt. This will exclude the harmless inactive scopolamine as well as the extremely dangerous apoatropine.

The objections of Hesse to the results obtained by Kobert, Schmidt, and Gadamer will hardly make any of them untenable.

Houdé gives the following data: "Scopolamine is the alkaloid of Scopolia japonica, a plant of the Solanaceæ family. It was first discovered in that plant by Langgaard. In 1890 A. Schmidt obtained it from the same, and also from Scopolia atropoides. It exists also in Scopolia lucida, a plant found in the Himalayas and in Nepaul.

"The substance designated by Bocquillon-Limousin as rotoine or scopoline, that which Van Renterghem and Dupuis designate as scopoleine, seems to us from the general description of its physical, chemical, pharmacologic and therapeutic properties to be nothing else than scopolamine.

"Scopolamine appears in crystals, fusible at 138° F. It is soluble in water, especially when slightly acidulated, very soluble in alcohol and ether. Its formula is $C_{17}H_{21}NO_4$. A. Schmidt put forth the hypothesis since his discovery in 1890 (see above), that this substance is possibly identical with hyoscine. But other authorities doubting this, Schmidt revised his experiments and distinguished

scopolamine from hyoscine, giving to the former the formula given above, and to hyoscine, according to Ladenburg, $C_{17}H_{23}NO_3$, which gives a very different chemical composition.

"Lately Schmidt and Hesse tried again to establish the identity of hyoscine and scopolamine, for both of which the single formula was to be $C_{18}H_{21}NO_4$. We cannot accept this opinion any more than that of Kradner, who tried to show before the Medical Congress of Livonia, that the hyoscine of commerce is nothing else than impure scopolamine, and hence the different action of the two substances, hyoscine provoking phenomena of intoxication while scopolamine does not.

"If we remember that scopolamine is a solid body, while hyoscine is of syrupy consistency, we can see even macroscopically that the two substances differ from each other notably enough.

"It is well to remember, that all those authors who propose this identification speak of the "hyoscine of commerce," that is German hyoscine. Now our readers will know from numerous previous proofs, that an alkaloid pure and chemically definite is far from a product delivered by German commerce under the name of an alkaloid.

"We maintain, therefore, the non-identity of scopolamine with hyoscine, and the following confirm the difference of their properties.

"1. Scopolamine raises the intravascular pressure by stimulating the vasomotor centers. This effect does not, however, take place in old people, and in those affected with aortic lesions, if we judge by the result of sphygmographic examination.

"2. Scopolamine exerts no appreciable influence on the respiration, and on striated muscles. It produces on the contrary a diminution of salivary and perspiratory secretions. Its use seems indicated in sialorrhea and profuse sudorrhea.

"3. Scopolamine diminishes cerebral excitability and so its action is the reverse of that of atropine. It acts as calmant and narcotic. It manifests its sedative action excellently when administered to agitated, demented patients in doses of a quarter to one milligram.

"4. The employment of this medicament gives good results in demented patients who are emaciating in consequence of the agitation to which they are a prey, and who disturb the repose of their attendants.

"5. When administered for some length of time the patients become accustomed to this drug and its employment is therefore contraindicated in persons with Bright's disease, in the aged, and in

cachectics. But the existence of a cardiac lesion does not counter-indicate the use of scopolamine.

"6. Scopolamine produces mydriasis and paralysis of accommodation, as well as a contraction of the bloodvessels of the iris and conjunctiva. Its mydriatic action is four or five times more pronounced than that of atropine. Moreover, no bad effects have been observed after using this medicament, which promises to do grand service in ophthalmic practice.

"7. Scopolamine is eliminated in the renal way."

Most of the conclusions arrived at by Rosistlay have been confirmed by other authorities. It can decidedly be said, that this medicament has the general property of diminishing the excitability of the cortical centers of the brain. It also paralyzes the action of the pneumogastric, which brings about the slowing of the respiration and an acceleration of the cardiac rhythm.

The vasodilating properties of this remedy show themselves in the rosy coloration of the face, in an augmented secretion of sweat, saliva, urine, etc., and by a mydriasis more or less accentuated.

On the brain its narcotic power is seen in the irresistible sleep without dreams or delirium. Its action is prompt at the end of four or five minutes.

Rahlmann experimented with scopolamine in eye diseases on the recommendation of Kobert, showing that it has a powerful mydriatic action, while internally administered it produces certain effects antagonistic to atropine. He concluded from the trials he made with scopolamine regarding its mydriatic and antiphlogistic actions, that it is superior to all other tropeins, that it is, moreover, free from the bad effects which are charged against atropine.

Ernst, a pupil of Kobert, arrived at analogous conclusions about scopolamine: It dilates the pupil, paralyzes accommodation, and induces contraction of the vessels of the iris and conjunctiva. In equal doses with atropine, scopolamine is four or five times stronger, and when perfectly pure has not the inconveniences of atropine.

The results obtained by Bellarminof agree also with those stated above.

As much, too, can be said of what Peters of Bonn says: Instillations made with a solution of scopolamine hydrobromide 0.02 percent produce mydriasis in a very short time as pronounced as that made with atropine.

Scopolamine does not diminish the intraocular pressure, and is also well sustained even when there is an increased pressure.

Peters confirms the fact that a prolonged use of scopolamine produces no dryness of the throat, no redness of the face, no nervous agitation, no acceleration of the pulse, all of which happen after the use of atropine and denote the commencement of intoxication. Peters also showed that scopolamine is well borne by those who have a decided idiosyncrasy against atropine, whether adults or infants. This applies also to flaxen blondes.

As a sedative, Bela Szalay, physician of a lunatic asylum at Pest, Hungary, experimented with scopolamine as a hypnotic, administering from half to two milligrams hypodermically. It was well supported, and its sedative action was constant, but the desired hypnotic effect could not be obtained. He says it can replace duboisine and hyoscine when the patient has become accustomed to these two medicaments.

Scopolamine possesses as much or less mydriatic properties as atropine in the treatment of iritis, keratitis, ulcers of the cornea, grave interstitial keratitis, and rheumatic iritis. It does not augment the intraocular pressure, it diminishes pain and never occasions any irritation.

Gutmann insisted that the toxicity of scopolamine is very slight, that he saw no intoxication symptoms after an instillation of even a 0.4 percent solution, while an instillation even with a 0.25 percent solution of hyoscine shows it plainly. Illig, considering the fact that the mydriatic effects of scopolamine are less durable than those from atropine, is of the opinion that the former should be reserved for subjects or cases which show great intolerance to atropine. When dilation of the pupil is needed for diagnostic purposes, Illig thinks cocaine should be used, as its mydriatic action is less enduring than that of scopolamine.

In recent iritis it is possible, according to Peters, to obtain a maximum dilation of the pupil and a rupture of the synechia by the instillation of a scopolamine solution of 0.2 percent. It is true that the mydriatic effect of scopolamine is less durable than that from atropine and that to maintain it at maximum will require frequent repetition. The same is true with the paralysis of accommodation from scopolamine. It is prompt in action but it lasts less long than that from atropine. Hence it is scopolamine that should, according to Peters, be used when mydriasis is needed for diagnostic purposes. But as to the salutary direct influence of scopolamine on the globe of the eye in inflammation, which Rhalmann affirms, Peters is uncertain, he not having had a sufficient number of cases in his practice to ascertain it.

Oldenrogue and Yourmann administered hypodermics of scopolamine hydrobromide from Gram 0.0002 to 0.0004 in cases of acute hallucinations, delirium tremens, acute mania, and gloomy vesania. The patients were chronic general paralytics suffering from insomnia, and were in a state of excitement. Except in the patients with delirium tremens, the scopolamine hypodermics acted very rapidly; at the end of five to fifteen minutes there came apathy, unsteadiness of gait, a sense of vacancy in the head, a somnolence, which soon passed into tranquil and profound sleep. The sleep is always accompanied by a considerable pupillary dilation, and the pulse becoming slow and full. The sleep came on rapidly and lasted from three to ten hours, according to the quantity of scopolamine administered. On waking the patients were more calm, did not complain of malaise, seemed to be yet under the calming effect of the medicament; but yet without somnolence.

The action of scopolamine shows itself especially rapid in maniacal excitement and in acute hallucinatory delirium. The patients become calm gradually, and fall asleep if the dose is somewhat larger. There was also some amelioration, although feeble in cases of melancholy with anguish, thanks to the regular sleep and slight apathy succeeding it.

In delirium tremens, however, neither scopolamine nor hyoscine had any influence whatever. There was no sleep even on Gram 0.0015 of scopolamine, all there was was feebleness, the patients continued in delirium, cried and were at times violent.

In chronic forms scopolamine is as efficacious as in acute; the irritability and insomnia cease on a hypodermic injection of the medicament, but in any case we have here to treat purely symptomatically. Among the secondary effects we have to notice are feebleness of the lower extremities, considerable mydriasis, lasting sometimes forty-eight hours and more, a considerable slowness of the heartbeat and an increase of the blood tension, which explains the decided diuresis present.

The repeated administration of scopolamine entails a slight habituation, but the increase of dose is hardly noticeable and the progress is very slow.

Ernst and Raechelmann advised not to use scopolamine in the aged nor in persons affected with renal trouble. But contrary to the authors mentioned above, Liepelt used scopolamine hydrobromide in patients with delirium tremens with success. In fever, delirium (typhoid pneumonia), and in intense motor excitements of other kinds, he also employed the medicament with success, and

administered in proper doses it seemed to be superior to morphine hydrochloride. It acted generally with certainty and gave no bad secondary effect.

Liepelt dissolves one centigram of scopolamine in ten parts of water. The solution must always be made fresh and clean, and given hypodermically, which is not painful. The dosage is to be calculated by the patient's state of excitement, his age, and above all by the weight of his body. Most often four to six milligrams are enough to obtain a calming effect, which makes its appearance and remains four or five hours. The medicament is always well tolerated.

The doses of this author are much larger than those of others. We believe it in place to follow here cautiously.

Rosistlay advises scopolamine in doses of one-fourth to one whole milligram. Bela Szalay advises one and one-half to two milligrams as a sedative in the demented and agitated; this last hypodermically. Oldenrogue and Yourmann say also hypodermically, but in doses of two to four-tenths of a milligram to begin with, and the dose of one-half milligram as the high dose which produces relaxation of the muscles. Only with the habituation which makes its gradual appearance are we obliged to gradually increase the dose, which should always be small at the beginning, viz., two to four-tenths of a milligram.

In ophthalmology Gutmann employs a collyrium of 0.2 percent, and he says that even with the strength of 0.4 percent he never met with an accident.

En resume.—(1) As a medicament in cerebral troubles, one-half to one and one-half milligram is the ordinary dose. (2) As an ophthalmic collyrium, 0.2 percent.

SCUTELLARIN

Standard granule—gr. 1-6, Gm. .01.

Scutellarin is a concentration from skullcap, Scutellaria lateriflora. It contains a glucoside obtained in acicular crystals by Myers.

Felter and Lloyd say that scutellaria is tonic, nervine and antispasmodic. It has proved especially useful in chorea, convulsions, tremors, intermittent fever, neuralgia, and many nervous affections. In delirium tremens it induces sleep. It is useful for the nervousness of teething children. In nervous excitability and restlessness or wakefulness, with or after acute or chronic maladies, from physi-

cal or mental overwork, or other causes, it is useful. It influences the cerebrospinal centers, controlling nervous irritation; hence its value in functional cardiac affections.

Specific Indications.—Nervousness, in or after diseases, or from exhaustion or teething; nervousness manifested by muscular action; tremors, subsultus, hysteria, inability to control muscles; functional cardiac disorders purely nervous, with intermittent pulse.

Ellingwood recommends scutellaria for paralysis agitans, and with cimicifuga in chorea; for insomnia from restlessness or excitability, and in prolonged fevers; it promotes sleep and stimulates the kidneys and skin to increased activity. The soothing effect continues after the remedy has been discontinued.

The writer has employed scutellarin to some extent, and finds it closely resembling cypripedin and valerian in effects. It is a mild, comforting nervous sedative, relieving nervous restlessness as well as the bromides and without their destructive effects upon the digestion and the vitality. In fact, this remedy should be classed as a nerve strengthener instead of a sedative. Subduing nervous irritability is not sedation but rather lifting the function up to a plane where it can act normally.

The dose of scutellarin is from one to five grains every hour till effect; the small dose is usually sufficient. Many times such a remedy is all that is desirable, and strychnine is not needed.

SENECIN

Standard granule—gr. 1-6, Gm. .01.

Senecin is a concentration from Senecio Jacoboea, or ragwort.

Two alkaloids have been found in this plant, senecine and senecionine. Bunch found that senecin caused a rise in the vascular pressure, with constriction of the peripheral blood vessels and those of the intestines. Under large doses the general pressure fell, the intestinal vessels dilated, and the contractions of the intestinal coats were inhibited. These effects were obtained from the alcoholic extract. The watery extract caused a fall of vascular pressure and cardiac inhibition (Shoemaker).

Senecin has been mainly employed as a regulator of menstruation; one of the popular titles of the plant being the Female Regulator. Delache and Heim found the solid extract act well, giving gr. 36 daily. Bardet and Bolognesis used it in 20 cases of amenorrhea and dysmenorrhea, and found it had the constant property of

inducing the menstrual flow and relieving the pain. Murrell speaks highly of this agent as an emmenagog, first treating the anemia and then giving senecin. One of the names of this plant is "old man," and it has been advised for impotence, with doubtful propriety.

Felter and Lloyd consider senecio of value in female disorders, relieving irritation and strengthening function; promoting menstruation when there is no structural lesion; in dysmenorrhea, sterility and chlorosis; in menorrhagia given during the intermenstrual interval and at ovulation; for tenesmic and painful micturition of either sex; leucorrhea with weakness of the vaginal walls allowing uterine displacement, with engorgement; male genital disorders with pelvic weight and full, tardy or difficult urination, and dragging sensation in the testicles; for tardy digestion from congested or relaxed gastric mucosa; capillary hemorrhages, hematuria, and bloody albuminuria; pulmonary hemorrhages; an excellent diuretic in gravel, etc., specific in strangury; dysentery.

Specific Indications.—Atony of reproductive organs with impaired function; uterine enlargement, uterine or cervical leucorrhea; difficult tenesmic urination; dragging in testicles; perineal weight and fulness.

Ellingwood says senecin works best in a general hyperemic irritable and atonic condition of the pelvic organs; the results are not immediate; in engorged conditions of the male sexual organs, impotence; an active diuretic; of value in gonorrhea and gleet, and prostatorrhea, sexual irritability of the male; overcomes conditions that cause food to lie heavy on the stomach; acts in harmony with viburnum, helonias, aralia, mitchella, etc.

In the trials the writer has made of senecin he has had no results whatever, from doses up to five grains a day. It is evidently requisite that much larger doses should be given, and as it does not act very quickly, the remedy should be continued for a month or more.

SODIUM SUCCINATE

Standard tablet—gr. v, Gm. .33.

Some twenty-five years ago the writer's attention was directed to sodium succinate as a remedy for gallstones. He commenced its use for that malady, giving five grains before each meal and at bedtime, and continuing its administration for a year. The paroxysms of the disease became gradually less frequent and less severe, until within the period named they ceased entirely.

This experience has been repeated in many cases seen by the writer since, and in all except two cases the above result has been attained. In one of these, a young woman with the intermittent febrile form, simulating malaria, the remedy was used intermittently and the test was not a fair one. In the other a physician came to the writer with the morphine habit from twenty-five years of this malady, and within a week the gall-bladder suppurated and surgical intervention was imperatively demanded. After years of suffering and many operations he is well. With these exceptions every case has recovered under the use of the succinate.

What does it do? We do not know. We have never had the opportunity to perform an autopsy on a man who had been taking the drug. Does it dissolve the calculi? We think not. Possibly it does. Does it subdue the catarrhal affection of the biliary passages and the duodenum? We think it does. It may act as an antiseptic or germicide, or in some other manner. All we know about it is comprised in the statement herein given. No theory is advanced; the practically unvarying success of twenty years is a phenomenon for the consideration and testing of our readers. As to the diagnosis, there have been a number of cases which had been diagnosed as gallstones by the first surgeons of the country, and the knife presented as the only treatment worth consideration—even the date set for operation; and yet these cases are among those which recovered on the succinate treatment.

Sodium succinate is not a remedy for the paroxysm.

Dr. W. H. Nunn writes that he attended a man with biliary calculi, and gave him the sodium succinate treatment. The man never had another paroxysm. Many cases have been reported to the writer where others have obtained results fully equal to his own.

In a case where the renal function was defective, the daily excretion of urinary solids being less than 300 grains, no other remedy proved as effective as sodium succinate. Under it—a scruple daily—the excretion more than doubled, with no ill effects.

SOLANINE HYDROCHLORIDE

Standard granule—gr. 1-67, Gm. 0.001.

While Bocquillon-Limousin terms solanine a glucoside he gives it the formula $C_{86}H_{71}NO_{32}$. It is found in the Solanum dulcamara, ferox, lycopersicum, Carolinense and nigrum, the young shoots of the potato and the tubers that have been exposed to the

light, and those that have sprouted, and possibly in Scopolia. The deeper layers of potato skins contain, at some periods of their growth, enough to cause toxic symptoms (Riley). Boiling water extracts the poison, and that in which potatoes have been boiled may prove toxic.

Solanine may be prepared by expressing the juice of etiolated potato germs, adding lime-milk or ammonia, in excess, which precipitates the solanine. This is separated by filtration, the insoluble part dried, and exhausted by boiling alcohol, which deposits crystallized solanine on cooling (Desfosses). It is a glucoside as dividing into glucose bodies, an alkaloid as to its basic properties (Merck).

Solanine occurs in fine, silky needles, colorless, possessing the properties of the alkaloids. It is insoluble in water, slightly soluble in ether and in cold alcohol. It melts at 240° F. It has a feeble alkaline reaction and forms salts with acids. Submitted to the action of boiling dilute mineral acids it splits into three equivalents of glucose and an alkaloid, solanidine, $C_{50}H_{41}NO_2$. Treated by an amalgam of sodium and water it gives nicotine, $C_{20}H_{14}N_2$, and butyric acid $C_8H_8O_4$.

Solanine has the property of forming a gelatinous mass with amyl alcohol when cold, even in the proportion of one part to 2,000. Cool amyl alcohol is the best solvent for solanine.

Brunton says that solanine in warm-blooded animals paralyzes the central nervous system without affecting the peripheral nerves or the voluntary muscles. It slows the heart and respiration, lessens sensibility, and causes death with convulsions. The temperature constantly falls. The pupil is unaffected. It produces weakness, labored breathing, nausea, vomiting and drowsiness, but no true sleep. There is no increase of action on the part of the bowels, kidneys or skin.

Nothnagel gives the formula of solanine as $C_{43}H_{71}NO_{16}$. It paralyzes the central nervous apparatus, causing general paralysis, reduces heart and lung action, and kills by asphyxial spasms. In man it also causes nausea and vomiting. French physicians have employed solanine as a nerve calmant, and analgesic, especially when it is desired to affect the medulla or the cord, as it lowers the irritability of both motor and sensory nerves.

Pictet gives the composition of solanine as $C_{22}H_{75}NO_{15}$. It contains no methoxyl, but six hydroxyl.

Spiegel, in Liebreich's Encyclopedia, gives the formula as $C_{52}H_{93}NO_{18}$ plus $4\frac{1}{2}$ H_2O. He designates it as an alkaloid. The salts are mostly amorphous and freely soluble in water or in alcohol.

Much water decomposes them, setting the base free. An amorphous alkaloid, solanine, accompanies it (Firbas). In the ripe potato there is but about 0.005 percent to be found, but in the eyes (sprouted) there may be as much as 0.5 percent. Solanine, like the rest of the saponine group, s an energetic protoplasmic poison, one percent in solution preventing the development of bacteria and the coagulation of the blood, and dissolving the blood elements (Perles). The lethal dose *per os* is 0.3 per kilo of body weight—3 to 10,000—and about 0.1 per kilo subcutaneously. In rabbits Husemann noted a reduction of temperature of over five degrees F., with muscular tremors, spasm of the jaw muscles, respiration rapid, then slowed, dyspnea and fall of cardiac energy. Then followed tonic-clonic convulsions, mydriasis and death from suffocation. The heart beat after the cessation of respiration, and stopped in diastole. He affirmed that solanine does not irritate the stomach, bowels or subcutaneous tissues, but Perles noted after intravenous injections severe enteritis, attributed to the poison excreted into the intestine; and also recent parenchymatous nephritis. The urine contained hemoglobin, methemoglobin, albumin, casts, and a few red blood cells.

Von Schroff found toxic symptoms in human beings follow doses of Gm. 0.2, or three grains; such as yawning, dizziness, stupor, somnolence but not sleep, tonic spasms, rapid small pulse, difficult respiration, nausea, salivation and extreme weakness. The effects of solanidine differ only in mydriasis and elevation of temperature.

Experimenting on animals, Perles found the same symptoms and post mortem appearances as after sapotoxin. Solanine did not cause diarrhea as the toxic plant did, possibly because the alkaloid was absorbed from the stomach while the crude plant was carried into the intestines. But solanine is more apt to affect the kidneys, as albumin and hemoglobin are generally found in the urine. Given to a dog, very little solanine or solanidine was found in the feces or urine, so that it is probably broken up in the body.

Caylus calls attention to the renal congestion caused by solanine and the plants containing it; also to the occasional diuresis, the tetanic spasms of the thoracic muscles, and increased sensitiveness of the cutaneous nerves; but he denies any direct influence upon the brain, stomach or bowels. He locates the action on the cord and medulla.

Solanine possesses an anesthetic power over the extremities of the pulmonary plexus, lessening the sensibility of the bronchial

mucosa, and slowing respiration. At first it moderates the pulse, then accelerates it. It irritates the stomach, large doses causing vomiting, colic and constipation. Small doses are laxative. It also possesses narcotic properties (Bocquillon-Limousin).

Cushny states that the action of solanine is almost identical with that of sapotoxin; solanidine differing only in not being a local irritant. While in potato sprouts growing in damp cellars the quantity of solanine rapidly increases, and it is also present in rotting potatoes, most cases of poisoning occur from the use of the small green unripe tubers that have been exposed to the sun at the surface of the ground. As the skins contain nearly half the solanine, if these are removed before boiling, much of the alkaloid in the edible part is removed by the water. The young buds arising from the potato contain enormous quantities of the poison.

Schmiedeberg describes an epidemic of potato poisoning, the symptoms being headache, colic, vomiting, diarrhea, depression, mental confusion, in severe cases pallor or cyanosis, dilated pupils, short periods of unconsciousness with rapid and then slow pulse, and in many cases a rise of temperature. All recovered within ten days.

In fatal cases of poisoning by plants containing solanine as their toxic principle, it has caused gastrointestinal irritation; an acrid burning sensation in the throat as the first symptom, followed by great restlessness, muscular and fibrillary tremors, labored respiration, dryness and hyperesthesia of the skin, rapid pulse, collapse and coma, the temperature falling markedly before death. The pupils are generally dilated. Albuminuria is usual. The fatal dose is unknown, but six grains would probably be uniformly fatal. The stomach should be washed out, after emptying it, strong tea or coffee given, the temperature sustained by artificial warmth, and opiates used for gastrointestinal irritation. Pilocarpine is said to have given good results. There is no chemical antidote (Riley).

Pfuhl saw many cases of poisoning among soldiers who had eaten toxic potatoes. Fifty-six showed similar symptoms, such as chills, fever to 100° and 103° F., headache, violent colic, diarrhea, severe fatigue, sometimes nausea, vomiting and fainting. Slight jaundice was present in some. The fever declined within three days, and recovery ensued. The treatment consisted in rest in bed, an ice-bag to the head, warmth to the abdomen, calomel, mint tea and opiates. The potatoes contained six times the usual quantity of solanine. It is not stated whether they were sprouted,

green or rotten. In the latter case another element would enter besides the solanine—the products of decomposition.

Geneuil recommended solanine as a substitute for morphine as an analgesic in neuralgia, gastralgia and rheumatism, but the action was not reliable. This is true also as to Sarda's application of it in diseases of the central nervous system; and Fronmueller's in agrypnia. But in symptomatic and hysteric asthma, and in whooping-cough, Clarus and Capparoni found solanine reliable. The action here is both direct and reflex upon the nerve centers.

Desnos employed solanine for painful maladies of the stomach, in doses of gr. 3-4 half an hour before meals, with benefit in gastralgia, painful dyspepsia, alcoholic gastritis with or without dilatation of the stomach, gastric ulcer and cancer. It has also proved useful in neuralgia, locomotor ataxia, asthma, muscular rheumatism (myalgia), chronic bronchitis, and the vomiting of pregnancy (Shoemaker).

Solanine has been employed against sciatica, neuralgia, rheumatism, gout, cystitis, cardiac asthma, bronchitis, whooping-cough, all spasmodic affections, pains of the stomach, dyspepsia and prurigo (Bocquillon-Limousin).

Caylus recommends solanine acetate in doses of gr. 1-6 to 1 for pulmonary maladies with spasm or irritation.

Constantine Paul recommended solanine in doses of a decigram —gr. 1 1-2—in pill, cachet or syrup. Hypodermically he gave solanine gr. 20; acid hydrochloric gtt. two; distilled water to five drams—15 minims containing gr. 1 1-2 at a dose. But Bocquillon-Limousin undoubtedly employed a better product, for he places the dose for an entire day at from gr. 1-4 to 1-2.

Merck gives the dose of solanine and the hydrochlorate as Gram 0.01 to 0.06—gr. 1-6 to 1—as a single dose; maximum 0.1 per dose, 0.5 per diem—gr. 1 1-2 per dose, 7 1-2 per diem. He suggests tannin as an antidote. Hypodermically the hydrochloride may be given in watery solution up to gr. 5-6 at a dose.

Spiegel gives the dose of the hydrochloride or the acetate as Gram 0.04 to 0.08—gr. 2-3 to 1-13—three or four times a day.

The first evidence of solanine action seems to be the acrid burning in the throat, decided toxic action being denoted by oppression of the respiration. The first-named symptom then, would indicate the full therapeutic effect, and the remedy should then be discontinued or given only as this symptom subsides. The alkaloid is very soluble as a salt, and hence its effects are quickly manifested. The proper adult dose may therefore be placed at gr. 1-12,

to be repeated every half hour till the burning throat indicates full effect. Or, a granule containing gr. 1-24 might be given every ten minutes for the acute pains of neuralgia or the paroxysm of asthma. For children with whooping-cough gr. 1-67 every half to two hours would seem to be the proper dosage to begin with; increased as per effects. Solanine poisoning should be treated by atropine and strychnine after emptying the stomach. The effects do not last very long, but just how long is yet to be determined.

Of the plants containing solanine dulcamara is probably that most frequently employed. It contains also an alkaloid dulcamarine, whose properties are unknown (Brunton). Poisoning by dulcamara causes skin eruptions with duskiness and itching; vomiting, dizziness, convulsions, abdominal pains, thirst, heat and dryness of the throat, rapid respiration and pulse, and vital prostration. In ordinary doses it acts as a sedative and mild narcotic. A distinct anaphrodisiac effect has been noted. Overdoses call for washing out the stomach with warm water and mustard, hypodermics of morphine and atropine, and diffusible stimulants by the mouth. Dulcamara is thought to be of service in scaly skin diseases, the recent decoction in rheumatism, and acute respiratory catarrhs; the extract has been given for mania, especially nymphomania and satyriasis (Shoemaker).

Ellingwood recommends dulcamara for acute respiratory catarrhs, pulmonary congestion, chest pain, an excellent auxiliary in acute bronchitis; usefully influencing the cutaneous manifestations of syphilis and scrofula; nervous irritation with depression, hyperesthesia, pruritus pudendi; give small doses and increase.

Dulcamara has been employed in scaly skin diseases, with antimony; and Husemann recommended it in chronic bronchial catarrh, asthma and whooping-cough (Brunton).

Lloyd terms dulcamara a mild narcotic, diuretic, alterative, diaphoretic and discutient; depressing the circulation in some persons, with lividity of the skin, dizziness and heaviness of the head, besides the symptoms elsewhere described as due to solanine.

Lloyd recommends dulcamara for mania with powerful sexual excitation; though it is said to occasion venereal desires, with heat and itching of the female genitals, and strangury; acute troubles due to colds; chronic skin diseases, pustular, vesicular, or scaly syphilis, rheumatism, cachexias, ill-conditioned ulcers, scrofula, indurations from milk, leucorrhea, jaundice, obstructed menstruation; especially scaly affections like leprosy, tetter, eczema and porrigo, with guaiac and yellow dock; for catarrhs give fractional

doses; suppressed menses with headache, nausea and chilly sensations, from exposure to cold; dyspnea, cough and chest pain from exposure; headache from acute catarrh, coryza, retrocedent and tardy eruptions; vesical catarrh aggravated by dampness; catarrhal diarrhea of children, rheumatism in those living in damp dwellings; nymphomania and satyriasis (Dewees); small doses for pudendal itching and stitching pains; small doses for chronics with feeble circulation, cold hands and feet, full tissues and tendency to edema (Scudder); the specific indications being: Scaly skin affections, acute disorders due to cold and damp, deficient capillary circulation in the skin, diminished cutaneous action with urinous odor, cold and blue extremities, full tissues with tendency to edema.

Solanum Carolinense, the horse nettle, has been highly praised as a remedy for epilepsy. It depends on solanine mainly for its therapeutic value. In large doses the horse nettle depresses the cerebrum and respiration, stimulates the spinal cord, but does not affect the circulation (Thornton). It is diuretic, anodyne and antispasmodic; of use in various convulsions and in tetanus (Napier).

Hare reported some success after a brief trial. It is not toxic like the bromides, though Wilcox and Stevens state that even in moderate doses, it causes marked hebetude.

Lloyd isolated from Solanum Carolinense an alkaloid differing notably from solanine, which he named solnine. Its properties do not seem to have been studied.

Lloyd says that horse nettle has been employed for tetanus, chorea, eclampsia, infantile and hysterical convulsions; its chief use being for epilepsy, especially the form where the paroxysms are worst about the menstrual periods.

Ellingwood recommends that in epilepsy the horse nettle be given until a sense of dulness or drowsiness is felt.

Dulcamara and horse nettle may safely be laid aside for the alkaloid solanine on which their therapeutic values depend. Especially in epilepsy and in cognate disorders should this agent receive a full trial, being pushed, as Ellingwood suggests, until full physiologic effects are manifested. So many reports have been made as to the value of dulcamara, that we believe its alkaloid will prove a worthy addition to our list of remedies.

In his study of the medicinal properties and uses of the most important of these alkaloids, Dr. Thrush speaks as follows:

"Solanum has been used extensively for a number of years by the negroes in the southern States in the treatment of epilepsy and with excellent results, as has been confirmed by a number of ob-

servers. It has been used in hysterical convulsions with prompt results, also in a case of eclampsia, in which it controlled the convulsions after everything else had failed. It has proven valuable in Bright's disease when the kidneys were acting but slightly and the patient was taken with convulsions; it completely controlled the convulsions, besides being an anodyne and antispasmodic, also a valuable and active diuretic. It is efficient in controlling epileptic convulsions attending painful menstruation, also epileptic attacks associated with imperfect development, chorea and puerperal eclampsia. It has been used with much success in pregnancy with convulsions due to albuminuria, also in uterine hemorrhage, and it acts as a powerful styptic in arresting hemorrhage.

"In order to obtain satisfactory results, the remedy should be carried to its full constitutional effect, which is indicated by drowsiness and stupor, then reduce the dose. It has been used with good results in tetanus and neurasthenia, and it appears to restore the want of equilibrium between the gray and white matter of the spinal cord. It does not affect the epigastrium like the bromides.

"Solanine is used instead of morphine in neuralgic affections, the vomiting of pregnancy, in bronchitis and asthma. Desnos recommended the administration of solanine to persons addicted to the morphine habit in place of morphine, when a sedative is required. According to him it is a valuable remedy in painful diseases of the stomach, similar in its action to cocaine and chloroform water. It is well adapted to individuals who easily become accustomed to morphine (hysterics and inebriates). Solanine is a poison to the terminal motor plates. It narcotizes the medulla and spinal cord, causing a paralysis of the terminal sensory and motor nerves. By reason of this, solanine is to be classed among the best of analgesics. It may be prescribed in large doses without danger, as it presents none of the inconveniences of morphine and atropine. and there is no danger of an accumulative action. It does not cause congestion of the brain, even in the aged, and probably a like freedom exists in children. In all cases in which it is necessary to calm excitement, relieve pain or overcome spasms, it promises excellent results. It may be given with advantage in place of morphine to relieve any of these conditions."

It is as a remedy for epilepsy that solanum has been most highly extolled. A number of observers have obtained excellent results from this drug, used to replace the bromides. It diminishes the severity and frequency of the attacks and seems to be entirely free from the distressing side and after effects which render the

bromides so objectionable. Pearce, in his "Diseases of theNervous System," says: "The berries of the horse-nettle, or Solanum Carolinense, especially in the form of the fluid extract, I have found beneficial in a number of cases of idiopathic epilepsy where there is no hereditary taint." And again he says, "After all other methods have failed, a fluid extract of the berries, pushed to a dram four times a day, has prevented an attack for three months, whereas the girl had been having them previously on an average of one attack every ninth day."

Spratling, Medical Director of the Craig Colony, New York, says: "I recall several cases in which Solanum Carolinense (horse-nettle berries) worked remarkably well after about everything else had failed." Other clinicians give similar testimony.

The most careful report made of the use of this drug in epilepsy, so far as we have been able to find, is that of Dr. Thrush. A series of twenty-five cases of epilepsy were treated by him with it in three Philadelphia hospitals. In these cases the fluid extract of the fruit and root were mainly employed. His results were tabulated as follows:

"1. It is of greatest value (probably better than any one known remedy) in *grand mal* of idiopathic type without hereditary taint, and where the disease has begun beyond the age of childhood.

"2. It is perhaps next of greatest value in hysteroepilepsy with marked convulsive seizures. In cases of *petit mal* the drug does not seem to do the great good that we have noted in the major type of the disease.

"3. In cases of well-advanced epilepsy of any type in which there is degeneration of the cerebral neuron, the drug will act specifically for a time, even better than the bromides, but it will finally be determined that the bromide salts will ultimately control the attacks better in these cases.

"4. The foregoing clinical study has brought out sufficient clinical evidence to warrant the statement that the inherent advantage of vegetable depressomotors is great as compared with any mineral salt given with the same intent, since destruction of the blood corpuscles by the latter is a most detrimental feature towards lessening the resistance of the individual in a disease where, above all, the constitutional tonicity should be favored as ideal treatment.

"5. A thorough impregnation of the nerve cells can alone be had, and therefore cure hoped for in epilepsy, in proportion as solanum is pushed to the fullest physiological dosage, and maintained through periods of months, a year not being too short a time to warrant its discontinuance.

"6. The fluid extract of the drug made freshly is the ideal form of pharmaceutical preparation, given in ascending doses, commencing with one fluid dram, and increasing to the full constitutional effect. It is to be decidedly preferred to the bromides in those cases in which it can be used advantageously, because no toxic symptoms follow its free administration, and the mental faculties are not impaired by its use."

A study of these reports must convince the reader of the value of this drug—but why the fluid extract? Why not the alkaloid? These questions naturally suggest themselves after noting the clear statement of Prof. Thrush concerning the alkaloidal content of the parent plant and the remarkable effects which follow the use of solanine. There can be no question that the virtues of the remedy reside in this alkaloid, solanine, and this has been clearly demonstrated by my own clinical experience and that of my coworkers and friends. In the light of this I feel safe in saying that in this alkaloid we have a much more certain and dependable remedy than the crude drug, one which when given with discretion in properly selected cases, always "to effect," will greatly alleviate and when used in association with other appropriate remedies will cure many of these distressing cases.

What are the evidences of physiological effect? As already said by Dr. Thrush, this is indicated by drowsiness and stupor, beyond which point the drug should not be carried. When this point is reached the dose should be slightly reduced and continued just beneath the point of tolerance. The suggestion of Dr. Waugh concerning the "acrid burning in the throat" should also be carefully noted as a guide to dosage. As will be noted the physiological action of solanine closely parallels that of the bromides, but minus their disadvantages. Solanine is a safe remedy, one which will not cause any dulling of mentality, nor when given in proper dosage, even such disagreeable minor symptoms as acne and digestive derangement.

Do not, however, make the mistake of seeking in solanine a "specific" or a "cure" for epilepsy. It is an adjuvant, merely, just as the bromides are adjuvants, to other and more essential measures. Perhaps no single remedy can do more—but it will not accomplish everything. Fundamental, here, as in so many other diseases, is toxemia. While the metabolism of this disease is obscure, we are more and more convinced, with our increasing experience, of the truth of this statement—the details of which were so ably and elaborately brought out by Dr. George H. Candler. And in the vast

majority of cases the *fons et origo* of the deranged metabolism is to be found in the digestive tract. Spratling and others have clearly shown the relationship between overeating and improper food and the frequency of the epileptic seizures, and have demonstrated the marvelous improvement which will often follow the rigidly enforced non-stimulating and restricted diet. This gives the key to the essential treatment, a key which we are surprised that more physicians do not use. We insist and urge that elimination is of paramount importance, or as we have so often advocated, "the clean-out and keep-clean idea." Of course this is not all: Hereditary influences, nervous instability, reflex irritations, especially those affecting the genital sphere, intercurrent disease, unfavorable environment, all these must be taken into consideration as links in the vicious chain. But we are reminded of a statement made we think by Burggraeve, that if to any disease there are several causes, remove *one* and the effect ceases. There is a large modicum of truth in this.

The treatment we suggest in these cases therefore includes thorough emptying of the bowel with calomel (associated with podophyllin, iridin, or other hepatic stimulants), to be followed by a saline laxative; the saline should be given daily for a sufficiently extended period to assure thorough cleanliness. Colonic accumulations may require enemata. Keep the bowel clean with the sulphocarbolates. The liver must be kept in the best possible condition with bilein and boldine; it is the great disintoxicating gland. Use proper digestive aids when required, such as pepsin, papayotin, quassin, etc. For nerve building use lecithin, a remedy which plays a most important part in the treatment of epilepsy. Use proper remedies to strengthen the heart, to enhance cellular nutrition, to improve the quality of the blood. Treat any intercurrent defect, such as nasal or ocular troubles, sexual diseases—anything which may prevent perfect physical health. And above all insist upon the most severe supervision of the diet, habits, sexual life and work of the patient.

But replace the bromides with solanine. Once the essential and exciting causes have been kept under control by measures just described this remedy may be depended upon to arrest or modify the paroxysmal attacks, and in cases amenable to treatment arrest their progress and not infrequently contribute to a complete cure of the disease.

The dose of solanine, as given by various authors, varies widely. Bocquillon-Limousin places the dose for the entire day

at 1-4 to 1-2 grain, while Merck and others give at each dose from 1-6 to 1 grain, or as high as 7 1-2 gr. a day. The rational way to administer it is to commence with small doses, one to six granules 1-67 grain, increasing the dose gradually until the point of tolerance is reached, then to maintain the dose slightly below this. Here again our maxim, "dose to effect," comes in. Success will follow it.

Solanine has a demonstrated therapeutic value, not by any means limited to epilepsy. It deserves further trial in tetanus, whooping-cough, asthma, in painful maladies (especially those of a spasmodic character) as a mild analgesic, etc. I urge its use in all such cases, and trust that fuller reports may soon be forthcoming. But as regards epilepsy its value is so striking, so well demonstrated, that I feel justified in most earnestly urging every reader to give it a trial, associated, of course, with other appropriate remedies.

French calls in question the dosage of solanine. He quotes Waugh as stating that the first evidence of the full therapeutic action of solanine seems to be an "acid burning in the throat," which is followed if the dose is increased by oppression of the respiration. "These symptoms, therefore, should be taken as indications calling for either a reduction in quantity or frequency, or else the entire withdrawal of the drug."

Thrush, however, states that in administering this remedy for epilepsy, "in order to obtain satisfactory results the remedy must be carried to its full constitutional effect, which is indicated by drowsiness or stupor, and then the dose may be reduced."

There is evidently here quite a diversity of views. As a general rule we advise that a remedy should be given until the first manifestations of toxic action are apparent, then the dose slightly reduced, believing that the full remedial effect of the drug is best obtained from doses just below those required to induce toxic action. It is becoming increasingly evident, however, that with many, if not all, drugs there is a decided antagonism between the effects of minute doses and those of maximum doses. According to Mays all drugs are probably stimulant in small doses and sedative in large doses.

Thus we have threefold dose-strengths from which to obtain the effects of a remedy, and it is a question not easy of solution as to which strength is preferable in any particular case. We have the stimulant effect from very minute doses, the full constitutional effect from the physiologic dose just below the toxic, and the sedative effect from the maximum dose, which may be stated as all that can be given the patient without endangering his life.

Which of these dosages gives the best results in epilepsy? If medicine is ever reduced to a perfect science, we shall know beforehand the reply to this question. At present we are unable to give any other reply than that the physician must try for himself and find out. Thrush evidently looks for the sedative-dosage effect.

In the case of absorbent remedies, like the iodine compounds, it is easy to see that when we are desirous of obtaining the utmost beneficial action possible from the drug, it will come from a dose which is able to stimulate the absorbents to carry away morbid material and yet is not quite large enough to cause the destruction of healthy, normal tissue-cells. Here the physiologic dose, just below that which would give rise to toxic effects, is exactly the one which we try to obtain. This is further exemplified by the administration of mercury in the treatment of syphilis; we try to keep as close to the salivation-point as possible, without actually touching it, to secure the most permanent and rapid effect upon the disease.

But that this is a general rule, applicable to all medicines, is another matter altogether. We may assume that it is, until experience has taught us better. It is a good general rule to go by in the administration of remedies; we holding ourselves ready at any time to modify this view with sufficient evidence.

In this way we avoid the danger, which is by no means small, of losing the effect of a remedy by giving it in ineffective doses. Jacobi has recently shown that this applies to digitalis as a remedy in feeble conditions of the heart; and *The Critic and Guide* has recently described a case in which this venerable clinician saved the patient's life by increasing the dose of digitalis fluid extract from one minim to ten minims.

But the question of dosage, when we attempt to dose to effect, is decidedly difficult. It is a trifling matter if we simply read in our books that the "dose is so and so," and give it; leaving the patient to get better or worse, making no alteration in this dose unless some unpleasant symptoms tell us to lessen it. If in due time the desired results have not been demonstrated we usually drop that drug altogether and take up another one which promises better.

When the habit of dosing to effect has been formed, we begin with a minimum dose, one too small in any possibility to do harm, and by rapidly repeating the doses we soon ascertain how much our patient will stand, or how much is necessary to produce the effect we desire. This dose once established it is easy enough afterwards to arrange it for more convenient administration into three or four doses each day.

Solanine is too new a remedy in the treatment of epilepsy to permit any one of us to speak absolutely. Our impression is that it is best to begin with small doses and push them up until the beginning of toxic effects warns us to discontinue the dose, or the effect upon the malady is such as we desire.

The few experiences of the writer have convinced him that the daily average dose for an epileptic is about one grain of this alkaloid. His opportunities for observations on the minute doses and the maximum doses have been too few to justify him in expressing an opinion. For these data we must look to the field. You gentlemen must not expect us to do everything.

SPARTEINE

Standard granules—Sulphate gr. 1-67, Gm. .001; gr. 1-6, Gm. .01.

Sparteine is an alkaloid derived from Cytisus scoparius, or broom. Broom tops contain the volatile liquid alkaloid sparteine, and a crystallizable neutral principle, scoparin.

Sparteine's chemical history was made up by M. Houdé, while the better mode of isolating the alkaloid is also due to him. Its physiology was studied by Laborde and upon its properties thus indicated Germain Sée introduced it into practice where it has redeemed all the promises its physiologic properties gave reason to expect. Hence sparteine is a remarkable confirmation of Gubler's axiom that therapeutics ought to be a corollary of physiology.

Sparteine becomes brown in the air. It is soluble in alcohol and in ether but not in water.

Scoparin has the formula $C_{20}H_{20}O_{10}$, forms yellow crystals, and has diuretic properties.

Sparteine has the formula $C_{15}H_{26}N_2$. It is derived from the mother-liquor from which scoparine has been crystallized. It is an oily liquid of penetrating odor and bitter taste.

Sparteine combines with acids to form easily crystallizable salts. The sulphate forms particularly large transparent rhombic crystals which are very soluble in water. It is the only sparteine salt employed in therapeutics.

One kilogram of the plant yields about 3 Grams of sparteine, by Houdé's process.

Physiologic Properties.—According to Laborde the main characteristic property of sparteine is an energetic stimulating influence on the heart, the pulsations of which it regulates while augmenting the energy of the cardiac contractions very rapidly. It

possesses a dynamic action over the heart, which is essentially of central origin, with the additional proper action on the intracardiac system of ganglionic nerves.

Four essential points characterize the physiologic action of sparteine: (1) Rapidity of action; (2) augmentation of energy, which it imparts to the heart; (3) regularity, which it induces in the contractions of that organ; (4) the absence of any effect upon blood-pressure, which it neither raises nor lowers.

The rapidity of the action of sparteine is such that it begins to manifest itself within fifteen or twenty minutes, and frequently even sooner, after its administration.

The increase of cardiac energy from sparteine is such that a pulse-curve tracing taken from a patient with an advanced valvular heart disease, while under the influence of sparteine, will scarcely differ from the tracings produced by a normal heart.

The regulation of the heart's pulsation by sparteine shows itself in more ways than one, according to circumstances. If the pulse-rate is below normal, sparteine will cause acceleration, but if above normal, it will bring it down to normal. Sparteine therefore rightly merits the qualificative designation of "cardiac metronome" which Laborde gave it.

The negative quality of sparteine, that of being indifferent to the pressure of the blood, neither increasing nor diminishing it, is recognized by all who have experimented with the remedy. This universally recognized quality is of great importance in therapy, and it is mentioned because precisely on account of this indifference it will have the preference in certain cardiac affections over other remedies.

This so remarkable action of sparteine upon the heart alone is still more remarkable on account of its intensity and persistence, since experiments on frogs show that the cardiac contractions actually continue even after the death of the animal and when its body is already beginning to stiffen. No other substance shows anything like such effects. The same results are obtained in experimenting with newly born dogs.

The results obtained show, moreover, that the action of sparteine is exerted directly on the muscular fibers of the heart, or rather on the intracardiac ganglionic apparatus, and in either case the action of sparteine is directly upon the heart without the intervention of the central nervous system. And this latter fact is most valuable in certain grave conditions of the patient when that system may be nearly incapable of reacting to the remedy or of

transmitting to the heart the impressions made by the remedy upon that system.

After Laborde and Legris had studied experimentally the physiologic properties of this remedy, and since Germain Sée applied it clinically, the physiologic facts of this remarkable remedy here given induced other investigators to study sparteine and thus secured for this remedy a specially marked place in the materia medica.

Garsonnin says that the natives of the Sahara desert dress snake-bites with a decoction of pounded twigs of the broom.

Antidotes are emetics and tannin.

Lewin observed that sparteine paralyzes the spinal cord, the motor nerves of the heart, and the inhibitory centers of the heart. In doses of 15 to 20 centigrams (2 1-2 to 3 1-3 grains) given to a warm-blooded animal it provokes difficulty in coordination-movements, somnolence, at first accelerated then dyspneic respiration, irregular heart-beat, convulsions, and death from paralysis of the respiratory centers.

The entire plant given to a human being provokes nausea, vomiting, diarrhea, palpitation, vertigo and headache.

Germain Sée, who applied sparteine sulphate to the treatment of cardiac affections, says of it:

1. It relieves the heart and pulse. It has a tonic action infinitely more marked, more prompt and more permanent than digitalis.

2. It has an immediate regularizing effect upon the rhythm of a troubled heart.

3. It accelerates the movements of the heart.

According to Richaut, however, it was noticed that although sparteine sulphate does accelerate the heart's movements and raises its energy, still it cannot regulate its rhythm when disturbed. Sparteine, therefore, according to this investigator, is neither an angiotonic nor a cardiotonic strictly comparable to digitalis; it can be preferred to the latter with benefit during the period while compensation is still being restored, or to replace digitalis when it has put things in order, but sparteine can not substitute the latter drug beneficially in a period when arrhythmia is confirmed.

Pouchet states that sparteine relieves the pulse and heart, regulates cardiac rhythm, and accelerates the heart-beat at least in a transient way. The effect is noticed half an hour after ingestion and lasts for three and four days after treatment was stopped. Its action on arterial tension is *nil* and the vasomotors are not

influenced by it. Sparteine continues and reinforces systolic impulses subsequent to the action of digitalis. Phenomena of accumulation are not noticed while it is being used.

The elimination of sparteine is easily effected by the kidneys even in patients with nephritis, and this makes it a valuable medicament in a great number of conditions, above all, cardiac cases. It possesses practically no diuretic action, but it *can* prolong a diuretic action previously effected.

The rapidity of sparteine-action is valuable in cardiopathic cases requiring prompt intervention to prevent asystoly. Moreover, even an exaggerated dose does not present near as much trouble as most cardiac medicaments do.

Sparteine would therefore, according to Pouchet, be most efficacious in recent cardiac affections while compensation is still maintained and degeneracy is but slight. Its indications comprise all cases of asthenia with an altered myocardium or an insufficient one, and where pulse is irregular, intermittent and arrhythmic.

According to this author the *entire plant* has a marked diuretic action owing to the scoparin it contains.

Guinard, Molliére and Vinay have used sulphate of sparteine locally applied to the skin and mucous surfaces in erysipelas, scarlatina, variola and measles, in which they had splendid results, especially in erysipelas, the remedy acting anesthetically locally and regulating the temperature at the same time, either elevating when too low, or lowering when too high.

The usual dose for an adult is from 5 to 10 centigrams a day. According to Burggraeve it can be given up to 20 centigrams a day.

Cushny says that sparteine closely resembles cicutine in its effects, the central nervous system being but little affected by the former, which paralyzes the peripheral motor nerve ends, and probably the terminations around the cells of the sympathetic ganglia. Sparteine depresses the heart more than cicutine, making the rhythm slow and contractions weak. It increases arterial tension less than cicutine. Sparteine is very much less toxic than cicutine or gelseminine. It kills by paralyzing the ends of the phrenic nerves in the diaphragm. The diuretic action of broom is due to the scoparin.

Sollmann classifies sparteine with gelseminine and cicutine. Its central action is weaker, its peripheral stronger than these. By vagus stimulation and direct depression of the cardiac muscle it slows and weakens the heart's contractions and lowers the vascular

pressure, because the cardiac depression overcomes the weaker vasoconstriction, which it causes. In some cases of asthma it is specific, in doses of gr. 1-6.

Pettey, however, has employed sparteine largely as a heart tonic, pushing the doses up to gr. 2, and he insists that this is the most powerful of all heart tonics, claiming that by substituting it for digitalis, etc., he has repeatedly saved lives. There is the possibility that in such cases the crude digitalis employed was so strong in digitoxin that the terminal arterioles were closed so as to render the heart's work impossible, and the discontinuance of this powerful toxin may have contributed to the cure. It is impossible to reconcile the discrepancy.

Sparteine lowers reflex action. Shoemaker says it raises arterial tension for five hours.

Cerna found it caused a brief period of increased muscular irritability and reflex action, followed by depression, spinal convulsions, generally tetanic, first increased and then depressed the heart's force and rate; similarly increasing and later depressing the blood pressure. Death is caused by paralysis of respiration. Sée asserted that sparteine promptly and strongly reduced the size of the heart. He gave it for weak and irregular heart-action, in doses of gr. 1-6 to 1-4 every four hours, especially in heart failure from mitral disease. In irregular heart action it proved serviceable. Gluzinski found doses under a grain best.

Satterthwaite says: "Convallaria has had its day. It has proved unreliable after extended experience. But sparteine has come into favor; though not so powerful a diuretic as digitalis, it is more prompt. I have used it satisfactorily both in heart failure and in cardiac dropsy. It may be necessary to give 1-2 grain before the diuretic effect is obtained, but it is not cumulative and I have never seen any ill effects from it.

Shoemaker speaks well of sparteine as a cardiac tonic, in the cases where digitalin is usually administered. It has been recommended in exophthalmic goiter, tobacco heart, to prevent uremia in angina pectoris, chorea with endocarditis, rheumatic heart diseases, the withdrawal symptoms following stoppage of morphine, as a preliminary to chloroform anesthesia in patients with weak or diseased hearts, to regulate the disturbed heart in young consumptives, etc.

There is here a curious contradiction. If sparteine can be given with advantage to the diseased hearts before chloroform anesthesia, there is hardly a doubt but that it acts as a cardiac tonic.

Possibly Cushny's conclusions are based on Schmiedeberg's experiments on animals with much larger doses than are given in the cases described. The writer has given sparteine as a cardiac tonic in doses below a grain a day, and found it especially beneficial in aged persons where it was necessary to continue the remedy longer than he cared to use digitalin.

Sparteine acts as a diuretic by increasing the vascular tension in small doses, as is the case with digitalin. Scoparin is a direct and powerful diuretic, increasing the quantity of urine and the excretion of urea.

A. S. Fulcher of California reports the case of a patient aged sixty, with enlarged heart and insufficiency of the mitral valve, who could not sleep owing to suffocation and pain in the chest, nor walk any distance without dyspnea. Various heart-remedies had given little improvement. Sparteine in two-grain doses every three hours soon brought relief, and in two weeks from first taking the remedy he went to work.

Stuart McGuire reports that he lost many more cases from post-operative suppression of urine, than from all other causes combined, until by accident he found the remedy in sparteine. This he gives hypodermically in doses of one to two grains, repeated every three to six hours. It increases the blood-pressure, makes the pulse slower and stronger, and acts as a diuretic. The effects are manifest within thirty minutes and last four to six hours. This observation is confirmed by Dr. Nicholson.

Dr. C. S. Cope, of Michigan, says: "It is to the doctor feeling his way carefully in his dangerous cases of heart disease that a new help in the drug line

> "Comes as welcome as the cry
> That told the Indian isles were nigh
> To the world-seeking Genoese:
> When the land breeze, from wood of palm,
> And orange groves, and fields of balm,
> Blew o'er the Haytien seas.

"In sparteine we have such a welcome help. It has an elective action all its own, and should be in every well-selected medicine case, standing shoulder to shoulder in bottled array with digitalin, apocynin, strophanthin, anemonin, strychnine, cornin, glonoin and cactin.

The following case will illustrate its helpful action:

"Case 1.—A lady, 50 years of age, has had valvular disease of the heart for ten years. Has at times been very dropsical; is anemic and neurasthenic. She is an "alkaloidist doctor's" wife, and her husband has by careful use of selected remedies successfully

carried her through many severe seizures when consulting physicians declared 'there was no hope.'

"During these ten years the vicissitudes of the menopause have come with the other storms that have sought to engulf this frail bark, but so well has she responded to the 'smallest possible dose' and 'just enough,' that a year ago she considered herself well, and was apparently as well and vigorous as any woman of her years. In January of this year, 1907, she contracted the grip and for nearly ninety days had a subnormal temperature and suffered from great debility and depression. She became emaciated and anemic, and angina pectoris came to assume the center of the stage. The case is typical. The least exertion, the movements of the arms, sudden excitement, will cause pain in the heart which radiates to the inside of the arms and stops at the wrists. These paroxysms are followed by extreme exhaustion.

"Now by many months of rest cure at her own home, the use of the 'heart-tonic' granules, tonics and a carefully regulated diet, she is really improving. There have been times when the heart tonic would not give its wonted help. Then it was found that sometimes cornin would relieve and later sparteine came as a God-send to the doctor in his gallant fight.

"Case 2.—A man, 56 years old, was brought to me from a distant state. He had been sick with an old heart trouble and dropsy; had not lain down in bed for four months. He was absolutely helpless and required the aid of four strong men to carry him from the baggage car, where he had to ride, to the carriage which took him home.

"I at once gave glonoin, strychnine and digitalin and began with a saturated solution of epsom salt, two tablespoonfuls every half hour. In thirty-six hours he had taken more than a pint of this solution. I also gave calomel and podophyllin, as his tongue was heavily coated. There was complete anuria. The kidneys had almost ceased to functionate. He breathed in gasps and required to be fanned all the time. His scrotum and penis were like huge bladders, fully distended. I plunged the trocar (without canula) into the end of the head of penis, deeply into the loose tissue, and when it was withdrawn the serum came out. In this way and without shock we have in three weeks drawn off a little over eight gallons of this dropsical fluid. The patient breathes easier and the kidneys are taking on normal action.

"He now gets, every four hours: apocynin, four granules; scillitin, four granules; calomel, 1-4 grain. These keep the kid-

neys and bowels in good condition. As a general tonic, strychnine nitrate, gr. 1-60, is administered every four hours; for the heart, sparteine two tablets, gr. 1-2 each, from two to three times a day.

"The patient is much improved. He was a high-liver and in former days a 'sport.' He called for alcoholic liquors which were interdicted, but Holland gin is given as needed. The dry diet is strictly enforced. The sparteine has a fine action in the case, the patient expressing great relief from his dyspnea while under its influence.

"Case 3 was reported to me by a physician who is a missionary just returned from a five years' sojourn in Central Africa. It is well known to those who practise in the tropics that the color of the blood in the veins and arteries is not so decided as is that of persons residing outside the torrid zone. This is probably due to the extreme heat and the lack of hemoglobin brought on by malarial and other poisons, so that the white resident, sooner or later, succumbs to debility, characterized by loss of vitality and weakened heart-action.

"The wife of the missionary was taken sick with a tropical fever more than a year ago and so fierce was the struggle it was feared she must die, but she survived only to find herself bed-ridden. She could not sit up because of a weak heart and the faintness that followed the effort. For many months they had been treating her and hoping for the day she should be able to start home, but she hardly held her own.

"Now comes a little story of the alkaloidal ministrations. When these missionaries were here, five years ago, I called their attention to *Clinical Medicine* and to the alkaloids and secured for them a copy of the journal and a year's subscription and a bill of alkaloidal goods, which reached them in three months from the time of sending. One day while reading the journal, they chanced upon an article on sparteine, and they both said: 'That seems good to us.' This was before the wife's illness. In making their order for goods from London, England, which comes once a year, they ordered one bottle of sparteine hypodermic tablets, as the coated granules do not hold up so well in hot climates. These goods arrived while the wife was ill, and having received the boxes the black boys soon removed the covers and the precious bottle of sparteine was found and a hypodermic given. The change for the better was apparent from that very moment. It had an elective action in this case surely; the pain and weakness were relieved and the convalescence hastened."

STILLINGIN

Standard granule—gr. 1-6, Gm. .c 1.

This remedy, representing Stillingia sylvatica, has won for itself the name of the "vegetable mercurial," and those who have watched its effects in syphilis consider it even more efficient than hydrargyrum.

One of the great drawbacks to the use of stillingia hitherto has been the unstable character of its preparations, neither aqueous nor alcoholic menstrua serving to preserve the drug principle any length of time. Stillingin, however, is unchangeable and gives the practician an effective, potent and evenly-acting remedy, while at the same time it well represents the fresh plant.

Stillingin may be termed (for want of a better word) an alterative *par excellence.* Alone, or with one of the salts of mercury or iodine, it gives prompt and visible results in scrofulous, syphilitic and tubercular conditions. Combined with phytolaccin it proves effective in goiter and tubercular glands; with rumicin and arsenic iodide it promptly causes the disappearance of scrofulous sores and, with proper local treatment, leg ulcers. It is one of our most potent aids to the successful treatment of syphilis. Whether given alone or in combination stillingin must be exhibited for prolonged periods and at the same time the patient requires and must have eliminatives and hematinics. The dosage varies: gr. 1-6 to 1-3 should be given every three or four hours—always to effect. It is an excellent drug to give to those syphilitics who are salivated. As far as experience serves, this remedy is most effective in the primary and secondary forms of syphilis, but is not out of place in the third degree, a state to which, early recognized and properly treated with modern antidotal and supportive remedies, few cases of syphilis need be allowed to attain. Combined with lobelin it may be given in alternation with calcium iodized in croup. Stillingin is also useful in bronchial affections in which there is tightness and irritation, but little or no expectoration. It soothes cough and promotes secretion.

The virtues of stillingia depend on an alkaloid, stillingine, of which Bocquillon-Limousin places the dose at 1 to 2 1-2 grains. It has been recommended in early cirrhosis of the liver, and for all the effects of defective function of that organ—hemorrhoids, indigestion, etc. The best available representative of this plant at present is a concentration, but the alkaloid will be furnished in due time.

STROPHANTHIN

Standard granule—gr. 1-500, Gm. .000125; gr. 1-134, Gm. .0005.

Strophanthin is a glucoside derived from Strophanthus hispidus, and some other species of strophanthus. Several principles have been isolated from the various species of strophanthus, and the name has been applied to derivatives differing in their strength even to the ratio of one to 90. It is absolutely essential that but one of these should be employed, to obtain uniformity and safety in its use. Arnaud's strophanthin has the formula $C_{21}H_{48}O_{12}$. Fraser considers it the only active principle of the plants, looking on strophanthidin as a decomposition product. Strophanthin is a crystallizable glucoside, soluble in water and in alcohol. It is a more powerful local anesthetic than cocaine. It causes passive congestion and may cloud the cornea if applied locally. It is bitter and in small doses promotes digestion. As a cardiac tonic it closely resembles digitalin, and a detailed account of its action would simply repeat what has been said at length under that head. The principal difference in their action is in the effect upon the vascular pressure, which is raised by digitalin much more than by strophanthin. In fact, the only increase in the arterial tension caused by the latter is what may be caused by the increase in the force of the heart and the consequent greater quantity of blood driven into the vessels.

Strophanthin does not disturb the digestion, nor has it any cumulative effect, that bugbear of the older physicians who did not employ the soluble digitalin. The tonic effect is not so enduring as that of digitalin. The quieting action on the nervous centers attributed to strophanthin is simply that seen after any cardiac tonic rightly administered.

If given continuously for some time diarrhea is apt to result.

Hatcher obtained results experimentally with strophanthus tincture, in ten to fifteen minutes after its injection. Wallace found that the tincture of strophanthus varied widely, as one specimen proved to be 200 times stronger than another. Strophanthin contracts only the mesenteric vessels. It does good within three hours. Hypodermically strophanthin is twelve times stronger than when given by the stomach. Intravenously it is seventeen times stronger. In a moderate typhoid hemorrhage strophanthin was given hypodermically; eight minutes later the patient sat up, complained of constriction of the heart, and died.

Loomis said strophanthus was one of the most unreliable drugs we had, and often inert. Of samples examined by the Board of Health of New York, sixty percent were inert.

Fraser specially recommended strophanthus in affections of the right heart, and of the aortic valve, when digitalin is contraindicated. Wilcox says success in its use demands a good preparation, its use in not too large or too frequent doses, avoidance of it in fully or over-compensated hearts, or in those presenting advanced muscular degeneration or mechanical defects of high degree. He considers it the drug of choice in all cases when we wish to establish compensation; all cases of arterial degeneration when more energetic cardiac contraction is required; all cardiac cases where diuresis is desired; all weak or irritable hearts; and all cases of heart disease in childhood or old age. This leaves little room for digitalin. But Balfour denies most of this, holding that when heart cases require anything beyond rest, they need a remedy to restore the elasticity of the heart muscle, and this digitalin does best.

Strophanthin has been advised in bronchial asthma, whooping-cough, hypodermically in chills of nervous character, malarial and urethral. Uremia and dyspnea of nephritis are relieved by this remedy. It has succeeded in exophthalmic goiter, when given in very large doses.

Satterthwaite says: "This glucoside is in my experience reliable, and in doses of 1-200 to 1-100 grain soon relieves dyspnea and precordial distress."

If strophanthin causes cold sweating and nausea, coffee and stimulants should be given.

Folia Therapeutica contributes an interesting note on the intravenous injection of strophanthin. The dose is one milligram (gr. 1-67). Fraenkel, after its use in fifty cases, reported that within a few minutes the pulse became strong, and the cyanotic symptoms were relieved very rapidly. The injections gave rise to no pain, but in a few cases rigors and pyrexia followed. Mendel's experience in five cases was less encouraging. In one the improvement lasted two days, and in three others no effects at all were produced. Schonheim used strophanthin in eight cases; his conclusions were:

1. An intravenous injection should be given in cases of cardiac failure which do not yield to ordinary medical measures.

2. Strophanthin raises the blood-pressure, produces diuresis, relieves congestion, but does not influence the pulse-rate. These effects last a few days and if necessary the injections may then be repeated.

3. In some cases rigors, giddiness, vomiting and headache may follow the injection, but subsiding in a few hours.

Hedinger had fifteen patients. His conclusions were:

1. Strophanthin acts quickly and effectively in cases of circulatory failure, as evidenced by his last series of cases.

2. The undesirable sequelæ, pyrexia and rigors, are due to bacterial contamination of the solution.

3. The effect of the injections does not become less as they are persisted with, unless of course the condition of the patient deteriorates rapidly.

4. In doses of 1 milligram every twenty-four hours there is no fear of any toxic cumulative action.

5. The intravenous injection of strophanthin possesses advantages over the administration of digitalis by the mouth.

The intravenous administration of strophanthin seems destined from most recent researches to displace the internal administration of digitalis. Strophanthin has a remarkable and certain effect upon the circulation when disturbances of the same are owing to cardiac affections. Side-effects from such administration of strophanthin there are none. Rise of temperature and chills, which were formerly observed, were owing to bacterial impurities which are eliminated at present. Frequently repeated injections do not diminish the effects except in so far as the nature of a progressing disease would bring with it. Cumulative effects do not appear if only one injection is given in twenty-four hours of one milligram of strophanthin.

The dose of strophanthin should be regulated by the effect on the pulse. One of the weaker granules may be given every hour or two till the desired cardiac tonicity has been attained, and then often enough to keep up this effect. If the stronger granules are used one every four to six hours is the dose for an adult at the beginning, and this should not be exceeded until the tolerance has been ascertained.

STRYCHNINE

Standard granules—Arsenate, gr. 1-134, Gm. .0005; gr. 1-67, Gm. .001; gr. 1-30, Gm. .002; hypophosphite gr. 1-134, Gm. .0005; nitrate gr. 1-67, Gm. .001; sulphate gr. 1-134, Gm. .0005; gr. 1-67, Gm. .001; gr. 1-30, Gm. .002; valerate gr. 1-134, Gm. .0005.

Strychnine is an alkaloid derived from Strychnos nux vomica. With it is found the closely allied alkaloid, brucine. In the same group we place thebaine, gelsemine, calabarine, laudanine, and curarine; while several other less known alkaloids are probably to

be placed here also. None of these has been studied as thoroughly as strychnine, and it is possible that each may sometime be found to fulfill some functions better than the others. Meanwhile strychnine has come into such general and extensive use that it behooves every practician to study its actions and powers to the fullest extent, that he may be able to recognize its effects, remedial and toxic, at a moment's notice.

Physiologic and Toxic Actions.—When a toxic dose of strychnine is taken the first effect is sharpening of the special senses, with stiffness of the muscles of neck and face. The reflexes are increased, and slight irritations cause quick and powerful movements. Tremors or twitchings of the extremities occur, and are followed by general convulsions, the extensors especially being thrown into action. The head is retracted and opisthotonos appears, with the sardonic grin. Respiratory spasm causes cyanosis. The muscular spasms alternate with relaxation, during which the reflex irritability is low. After two or three convulsions death occurs, the respiration not being resumed. In some cases the convulsions subside but death occurs from asphyxia. Very large doses cause death by paralysis of the nerve centers without convulsions.

The action is directed to the central nervous system. The cord is affected more than the cerebrum. The intellect is not directly affected and the pain is exquisite. Not only are the special senses made more acute but the field of vision is widened, and shades previously indistinguishable can be recognized.

The convulsions are due to stimulation of the spinal reflex function. They may be prevented by excluding external irritations. The tone of the medulla is increased by small doses, and affected by large ones as is the cord. The tendency to convulsions is lessened by rhythmic movements of any description. No direct effect is exerted on any of the voluntary muscles.

Large doses paralyze the motor nerve ends, by direct action. Small doses quicken and deepen the respirations. The heart is not directly affected by strychnine, but stimulation of the center of inhibition slightly slows it. The peripheral arterioles are contracted by stimulation of the vasoconstrictor center. Remedial doses raise the vascular pressure and slow the pulse. During convulsions the pressure rises very high, from the direct action and from the blood being forced out of the abdominal vessels by the violent contraction of the muscles. The vasoconstriction is greatest in the internal vessels, those of the skin and possibly the muscles being dilated. Cushny attributes this to stimulation of vasodilator centers in the

medulla. The heart beats long after respiration ceases, and artificial respiration may keep it beating indefinitely.

Strychnine acts on the stomach as the other bitter tonics, in small doses; and is absorbed from the intestine.

From the enormous increase of muscular activity strychnine raises correspondingly the excretion of carbonic acid and absorption of oxygen. No rise in temperature is caused, as the dissipation of heat through the skin is even more increased. The internal temperature falls a little while that of the skin rises. Even small doses cause the glycogen of the liver and muscles to disappear (Demant).

Strychnine is eliminated mainly by the kidneys, the process lasting a week or more. Part is excreted into the stomach and part oxidized in the tissues. The continued use of strychnine begets a certain degree of tolerance. Trousseau gave it in ascending doses up to and exceeding a grain a day, to adults. Man is more susceptible to it than animals, and the young are more susceptible than the old.

Strychnine stimulates the peristaltic movement of all the hollow viscera, intestines and bladder. Large doses may cause diarrhea. The pupil is dilated. Small doses promote the amylolytic action of the pancreatic juice while large doses suppress its secretion. The genital functions in both sexes, the menstrual flow, testicular secretion, erectile power and venereal appetite, are increased by strychnine.

Baglioni determined that the action of strychnine is exerted on the sensory cells of the spinal cord and not on the motor cells. The action consists in facilitating the passage of the nervous impulse through the sensory paths, so that slight irritation induces exaggerated motor responses. Touch offers the most effective irritation, especially of the skin. Sollmann says that the location of the strychnine action in the cord explains why its convulsions are abolished by curare, which blocks impulses from the cord to the muscles; also why strychnine acts more on a paralyzed limb when the lesion is above the cord, for the reflex is then more pronounced. The improved muscular tone is due to the heightening of reflex irritability. Other spinal centers being stimulated explains the value of strychnine in impotence, sphincter paralysis, etc., when due to lowered activity of their spinal centers. The increased muscular activity induces pain, increases metabolism, rise of vascular pressure, faster pulse if not balanced by vagus stimulation, rise of temperature if not compensated by dilation of cutaneous vessels and increased radiation, asphyxia at first by tetanizing the

muscles and later by depressing the center. This asphyxia causes venous congestion, cyanosis, lividity, protrusion of eyes, more convulsions and rising pressure; also glycosuria, the liver glycogen disappearing. As asphyxia is prominent the need for artificial respiration to prolong life is evident.

Sollmann asserts that the continued use of strychnine does not beget any tolerance, and that it is better borne by the young than by the old. Both assertions are contrary to other observers, and to clinical trials. An exception may be made when the aged are subject to arteriosclerosis, or to fatty heart, or display abnormal vascular tension, but not otherwise.

In its action on the nervous centers strychnine is synergized by caffeine and picrotoxin; these acting more upon the cerebrum. Morphine aids its action in increasing reflex irritability, curare aids action on the ends of striated muscle. The action on the cervical sympathetic ganglion is allied to that of nicotine, while the cardiac toxic effect is aided by many toxins. As a respiratory stimulant atropine synergizes it, while aconitine and large doses of strychnine incite cardiac inhibition.

Toxic symptoms appear between fifteen and thirty minutes after the dose has been taken, rarely being delayed. Death usually comes within half an hour of the first attack. Sollmann advises permanganate and iodine as antidotes, or tannin, but not coffee. The physiologic antidotes are chloral, chloroform and paraldehyde. Perfect quiet and artificial respiration are essential.

The absorption of strychnine is more rapid when given by the rectum than by the stomach. The elimination of this drug by the saliva and other alimentary secretions tends to accumulate it in the system as it is reabsorbed from the lower bowel. Stocker found flushing of the face, throbbing head, vertigo and faintness to be the evidences of beginning toxic action, or saturation.

The slowness of its absorption and elimination renders it wise to suspend the use of strychnine for intervals. It inhibits the movements of the leucocytes, though much less than quinine. A bright red eruption is mentioned by Shoemaker as having been exceptionally caused by strychnine.

Death has resulted from half a grain of strychnine, and from three grains of extract of nux vomica; but six grains of strychnine have been taken without the fatal result. Recovery is the rule if the patient survives three hours.

One observation made by the writer he believes may be of importance. Coming out of a warm room late on a very cold night—

below zero—very tired, he took two granules of strychnine sulphate, each gr. 1-30, to sustain his fatigued limbs for the walk home. In a few moments he was overcome by a sense of muscular weakness so that his legs could scarcely sustain or carry him. It was with some difficulty he kept up till he reached home. It can be readily seen how another dose might have proved perilous in the extreme.

Falconer reported a case of chronic poisoning, the symptoms being extreme weakness, muscular pains, stiffness of the back of the neck, clonic convulsions of the forearm with contractures of the finger flexors, vertigo, amblyopia, and weak but regular pulse. The patient had taken gr. 1-30 four times a day for eight months up to her death.

The diagnosis of strychnine poisoning may be made by the tonic convulsions, never clonic as in epilepsy; the jaw is not first attacked as in tetanus; in tetany other than the cervical muscles are affected with persistent rigidity; in hysteria the contractions are painless, and the history and aspect of the case are radically different; in hydrophobia the mind is affected, and the history and duration of the attack differ.

The chemical antidote to strychnine is tannic acid. Shoemaker speaks of cold tea or coffee as being quickly available forms. The stomach should be soon washed out or vomiting induced, as the tannate of strychnine is slowly soluble. Anesthetize the convulsed patient before trying any manipulation. The chloral group are antidotes, but pilocarpine and probably physostigmine synergize strychnine. Relaxants are antagonistic, such as tobacco, alcohol, cicutine, morphine, glonoin, etc. Turner claimed that lard was a remedy, but this seems to be simply a means of delaying absorption.

Therapeutics.—Strychnine stands at the head of remedies for poisoning from venomous snakes, of all varieties. One effect of the venom is paralysis of the vasoconstrictors of the abdominal vessels, by which the blood from the whole body is heaped up in the abdomen, and the patient dies from cerebral anemia. This effect is directly antagonized by strychnine. It must be given in full toxic doses and repeated as required, without reference to its ordinary dosage. The discoverer urged from gr. 1-5 to 1-3 hypodermically as a first dose, and then enough to keep up the toxic rigidity thus induced. Failures are due to the fear or carelessness by which this dosage for effect is not maintained until the danger is past. The paralysis keeps recurring for days perhaps, and the dosage requires intelligent, fearless and persistent repetition.

The close similarity between the symptoms of snake poison and those of the Amanita phalloides, the deadliest of poisonous mushrooms, has led to the use of strychnine. This is strictly correct in principle and we may expect good results. A somewhat similar condition exists in persons overcome by enormous quantities of alcohol. The hypodermic use of enough strychnine affords the best chance of saving the life.

In doses of gr. 1-67 any of the salts of strychnine forms a good bitter tonic for weak digestions, but it is better to save this great remedy for great uses, and employ the equally efficient and far safer quassin for an appetizer. In very small doses, gr. 1-500 of the arsenate is best, it is useful for many forms of vomiting, that of pregnancy and of drunkards especially. Give the dose every hour till the patient is toned up enough. When alcohol has been used habitually and an effort is made to break off the habit, there is a miserable sense of debility, of utter prostration and nervelessness, mental and physical; and this is best met by strychnine in doses sufficient to put the whole system in tone, like a violin-string in tune. This may require but little, or enough to make the timid therapeutist, unaccustomed to dosage for effect, quake in his boots. Much or little, there is no danger from the remedy, if given as really needed; and too often the treatment fails from timidity or rashness. Capsicum is the best adjuvant.

Gastric catarrh and dilatation of the stomach are relieved by small doses of strychnine continued some weeks, with carefully regulated diet. No possible benefit can accrue from any medication if the patient continues to distend his stomach with food and cold drinks, etc. Berberine and physostigmine are useful aids.

Hemorrhoids and other evidences of an atonic state of the large bowel, are relieved by moderate doses of strychnine, with suitable diet and laxatives. Chronic diarrheas and dysenteries continuing from relaxation, often respond nicely to a little strychnine.

Lanphear calls attention to the alarming nervous depression frequently present in strangulated hernia. For this he recommends the injection of strychnine sulphate 1-15 grain. In a few minutes after this a tablet of H-M-C anesthetic may be injected; and by the time everything is ready for operation, which may often be done under cocaine, the general condition of the patient will be much improved.

W. J. Robinson reports excellent results from the administration of strychnine and hydrastine, in the bladder or prostatic urethra, for patients suffering from weakness of micturition.

In cardiac asthma there is no remedy comparable in effect to strychnine arsenate, if given to full toleration. This may require up to near a grain a day; but it is imperative that no more than actually needed be given. Sometimes it must be continued for months; but other measures, diet and regulated exercise, and climate, should be utilized so as to render the use of this priceless boon as limited as is actually necessary. For the true physician must ever distinguish between temporary improvement and actual cure; between the stimulant that rallies the last reserves, and a real increase in the vital forces.

And this last remark leads us to speak here of strychnine as a remedy for sexual weakness. It is a disaster for man or woman to get hold of this bit of information without the further knowledge that governs and corrects it. Humanity wants increased sex power, despite the notorious fact that many men and some women would be the better for having a good deal less. Strychnine cannot bring back youth, nor indeed increase the vital stock. It simply rallies the reserves, to be used wisely by the very few, to be more quickly wasted by the foolish many.

Strychnine fills an important place in the treatment of paralyses. When an apoplectic effusion has occurred, some nerve fibers are torn asunder, others are compressed by the effused blood, by the zone of inflammation surrounding the site of injury, and by the zone of edema surrounding that. Recovery from the compression from each goes on more slowly than in the zone outside. Some fibers do not resume their functions even when the pressure is removed. Strychnine comes in here, to arouse the nerves and restore their tone. In the latter respect it is better than electricity. It should not be given till the first period is past, in which we try to limit the effusion; nor in the second, when we are promoting its resorption; but after six weeks have elapsed we begin cautiously with small doses, and increase cautiously to full tolerance. And the word "cautiously" is here repeated purposely.

All forms of paralysis come under this treatment. Strychnine will do all that any medicine will, for these cases.

Sollmann says that strychnine is especially useful in paralyses from lesions above the cord, by maintaining the nutrition of the muscles and preventing atrophy. It also lessens the pain in old paralyses. It especially strengthens the sphincters, rather than the detrusors. In collapse and shock its dangers have been urged by Crile, and these apply to the large doses the terrified practician is too apt to use in such cases. Small graduated doses meet the need.

As a heart tonic strychnine is out of place. Whatever action it has here is confined to vascular contraction by which the heart's work is increased. The supposed benefits secured from it are attributable to the general incitement of the vital functions and the improvement of digestion.

Mays has urged strychnine as the chief remedy for phthisis; and as to its efficacy, when the alimentary canal has been rendered aseptic, there is no doubt. But we have not found in it any specific virtues.

Strychnine has been used with benefit in all forms of amaurosis, in neuralgias of all descriptions, where full doses often break up the pain habit, in chorea, epilepsy, etc.

Prof. A. B. Hughes, of Keokuk, treats of some unusual applications of strychnine, deducible from its physiologic effects.

The chief dynamic force of strychnine is expended upon the central nervous system, raising reflex irritability from the lowest portion of the cord upwards. Motor and sensory cells are specially stimulated (Sollmann). Blood pressure rises, metabolism increases, all the muscles of the body are stimulated. The stimulation of the pelvic organs renders strychnine an ideal aid to young girls at puberty. Raising muscular tone, it tends to strength of "constitution." Girls suffer from under muscular activity and over brain exercise; they are always tired, menses scanty and irregular, insomniac, given to fudges, and here strychnine in small doses, long continued, works a wonderful change—rapid and splendid development pelvically, healthy complexion, bright eye, rounded chest, erect form, and firm gait.

Given during the last month of pregnancy strychnine keeps the abdominal viscera up to their work, aids excretion by bowels and kidneys, prevents dropsy, and induces euphoria at labor. Acting on the cord, it strengthens the contractions, shortens labor, and promotes return to normal conditions later.

Strychnine antagonizes habit drugs; and is useful in treating these habits when pushed to the verge of toxicity.

Given during late pregnancy, strychnine must increase the vital resistance of the child, resulting in better growth and development. This has been verified by the writer's experience—the children are invariably strong, vigorous, and seemingly endowed with strong resisting powers.

A general tonic, one that improves the tone and increases the function of every tissue and organ in the human body, it would be strange indeed if it were not abused. We are now in the strychnine

epoch, when everybody gets strychnine for everything. Many a case of strychnine habit exists, as yet unrecognized. Many a case of chronic poisoning, we fear, goes to the grave unrecognized. The lazy doctor adds this to his morphine and whisky, and finds he has his needs amply supplied—with an occasional dose of salts. Against this tendency the best defense is the nicety of prescribing acquired through the use of the alkaloids. As one becomes accustomed to certainties in effects he needs more and more remedies by which exactness of indication may be met exactly therapeutically.

In treating the alcohol habit the nitrate of strychnine has been preferred to the other salts. It is quite soluble and easily given hypodermically.

The hypophosphite of strychnine has been advised when this remedy is employed as a reconstructive tonic, especially in the young, and when combined with other hypophosphites, of lime, iron, quinine, etc.

Strychnine arsenate combines the properties of these two great tonics, and is most extensively employed when vital incitation is indicated. The dose as to strychnine is about two-thirds as strong as the sulphate, hence the granule of gr. 1-67 equals about gr. 1-100 of the latter.

It has seemed to the writer that the response from strychnine valerate came more promptly than from any of the other salts. Small as is the quantity of valeric acid in the dose, it is not without activity, and in nervous and hysteric cases, and when given as a bracer, a restorer of tone in conditions of hypochondria, neurasthenia, spermatorrhea, and the consequences of mental overwork, this salt has proved eminently satisfactory.

In all but emergencies where it is essential to obtain maximal effects as quickly as possible, it is wise to use very small doses of strychnine and gradually repeat until the desired tonicity has been secured. This avoids all danger of overdosing, or of striking an idiosyncrasy, and begets in the physician the habit of closely watching his patient's symptoms, which is not so universal as one could wish. Even with alcoholics the response to strychnine may come with incredibly small doses; and on the other hand these people may require almost incredibly large doses to equalize the nervous pressure and restore that springlike tonicity that does so much to encourage them to persist in their reform. Many reformed inebriates emerge from the "cures" with the strychnine habit. This may be gradually shaded down into brucine, and this into berberine; but even if not, it is surely preferable to the whisky habit.

Troisfontaines advises that strychnine be employed in much larger doses than are usually given. He gives from 1-12 to 1-6 grain hypodermically as indicated, repeating up to a total amount of 3-10 to 6-10 grain in twenty-four hours. From such doses he has never seen untoward effects. He uses strychnine in diabetes mellitus, certain paralyses, sunstroke, psoriasis, pulmonary tuberculosis, surgical shock.

During the past decade strychnine has come generally into use as a means of sustaining the vital forces and the heart especially, during the course of fevers. In pneumonia it may be termed the chief reliance of many physicians. This matter has been fully discussed in the chapters on aconitine, digitalin and veratrine, to which the reader is referred. In all febrile maladies when there are any signs of adynamia approaching, the rule is to forestall danger by adding a sufficiency of strychnine; and many a life has been saved by this wise forethought. But that does not mean a senseless administration of this powerful drug where it is not needed. There is a place for veratrine as well as for strychnine.

In constipation strychnine is a useful ingredient of every really valuable combination for the cure of this malady.

And yet the half has not been said. Every physician of wide experience can add instances of the fitness of this most powerful agent for special conditions not mentioned in this article.

THIOSINAMINE

By treating oil of mustard with absolute alcohol and ammonia we obtain allyl sulphocarbamide or thiosinamine. The chemical formula is $CSNH_2NHC_3H_5$. It appears in the form of colorless crystals, bitter, of a faint garlic odor; slightly soluble in water, freely soluble in alcohol. It is an active stimulant of glandular and lymphatic activity. Boliker found the phagocytes abounding in scar tissue. Some hours after a hypodermic dose a marked fall occurs in the number of leucocytes, Hebra says from 14,000 to 4000. This is rapidly followed by hyperleucocytosis which endures as long as the remedy is being given. Local reactions occur about exudates and transudates, without general disturbance.

Hebra introduced thiosinamine for use when it is desired to excite local reaction in an inflamed, cicatricial or poorly nourished area; when glandular stimulation is desired, or hyperleucocytosis is indicated. He reported favorably on its use in treating lupus and old cicatrices; also chronic non-syphilitic glandular enlargements. An ectropion caused by lupus was cured.

Haus reported favorably on this remedy in urethral strictures, as did Tousey, who found that when aided by the occasional passage of a sound it cured cases usually amenable only to cutting operations. Lutzko tried it on uterine tumors, old perimetritis and salpingitis, finding the softening action undoubted; the tumors often growing smaller. Unna added his testimony as to its efficacy in cicatricial contractions, local tuberculosis and corneal opacities of long standing, which cleared up. Tousey declared thiosinamine possessed positive curative properties in resolving benign and malignant tumors, cicatricial tissues, keloid and corneal opacities. He also urged it for deafness due to tympanic embarrassment by fibrous tissue.

Hubbard advocated this remedy in catarrhal deafness, disseminated choroiditis, diffuse corneal opacity and senile cataract.

Unna applied thiosinamine locally for keloid, leprosy, and to remove smallpox scars.

Neisser obtained good results in scleroderma; as did Juliusberg in scars from lupus and burns.

Upon tried it in six cases of chronic joint disease; two were greatly improved, two affected doubtfully, two not at all.

Armstrong reported a cure of epithelioma recurring in a scar, from galvanofaradism, and the local use of thiosinamine and guaiacol.

Teleky got good results in two old cases of esophageal stricture.

Suker used thiosinamine internally for corneal opacities, cicatricial contractions of the eyelids after trachoma, exudative choroiditis, symblepharon, capsular opacities (post-operative), cicatricial ectropion and plastic iritis.

Sherman found it valuable in chronic vascular cicatricial keratitis, and Randolph got good results in obstinate tinnitus. Somers found it useful in sclerotic deafness, the benefit being manifest within six weeks if at all.

Kaufmann obtained most satisfactory results in a case of chronic gastric ulcer with tumorous proliferation.

Renon advised its use in arteriosclerosis.

Lermoyez employed it in purely adhesive cicatricial or catarrhal deafness. He applied thiosinamine by instillations through the eustachian tube or by irrigation of the canal; the only other treatment was systematic massage of the tympanum. Eight cases were benefited by this method. Every evening the patient's ear received a bath of a hot solution of thiosinamine antipyrin. Twice

a week he practised pneumatic massage of the tympanum. In general, by the fifteenth day there was a decided improvement in hearing, most marked in cases of cicatricial adhesions following cured otorrheas, or where a large perforation permitted the penetration of the solution into the tympanum. In refractory cases tubal injections were practised.

The solution caused neither pain nor irritation when injected. It consisted of 15 parts of thiosinamine, 7 1-2 parts of antipyrin and 100 parts of distilled water. The solution was sterilized and only two or three drops used at a time.

A very happy effect of this remedy is reported in *La Province Médicale:* "The case was that of a woman forty-seven years old, who after being attacked with very severe blennorrhagic rheumatism was left with an absolutely complete ankylosis of the knee, a stiffness of the shoulder joint and limited motion in the elbow, wrists and fingers. The articular motions of the hips and ankles were also limited and painful. After the failure of medical and surgical treatment, the administration of thiosinamine solution in the proportion of 1 in 25, prepared cold, was instituted. From the 10th of September to the 3rd of October the patient received twenty-five hypodermic injections each of 5 Cc. in the abdominal skin, which makes 20 centigrams of the remedy in solution. Immediately after the prick of the first injection the patient felt a taste of sulphur in the mouth, which was disagreeable and lasted for many hours and gradually disappeared. An amelioration of the joint trouble was felt on the eleventh day from the beginning of this treatment, and though the movements remained limited yet the patient declared the articulations were more supple and their mobilization occasioned no pain at all. The amelioration increased on the following days. On the twentieth day, however, the patient noticed an important and new fact, namely a particular difficulty in walking, although the articulations had regained in part their suppleness and the pains were very slight. It seemed to the patient as though the muscles were elongated and did not obey as in the past the incitation of the will. The muscles had lost their tonicity but were not paralyzed. In this case the action of thiosinamine shows itself both as a real ameliorator of articular troubles and also as having an unfavorable action on the voluntary muscles and the heart-muscle. The patient in this case was tainted with chronic rheumatism, general arteriosclerosis and latent myocarditis. We shall have to exercise care in cases like these, not to go beyond the point of relaxing the periarticular fibrous tissues lest we impair the voluntary muscular system."

Pollak says: "The much promising name of fibrolysin has been given to a substitute for thiosinamine, which latter has the disadvantage of being very painful when administered hypodermically after the customary formula. It can, however, be given perfectly painlessly by employing the following formula: Thiosinamine, Gram 1.0 (gr. 15); distilled water, Gram 5.0 (gr. 75); glycerin Gram 5.0 (gr. 75). Of this solution one Gram (gr. 15) can be injected unhesitatingly into a feeble person, and the pain will not be greater than from a similar injection of morphine or may be not more than from the prick of a needle. It may be that the single injection from the formula will produce a weaker result than that from the customary formula, but the advantage is that the injections can be made as frequently as five or six times a week without any drawbacks.

"That the same results can be achieved from the weak solutions as from the stronger is evident from the following history: Patient, a woman 36 years of age; in her third pregnancy in the fourth month; cough for many years; hemoptysis two years ago; first parturition four years ago was spontaneous, and the child died soon of convulsions; second pregnancy terminated with miscarriage in the fourth month; patient has complained for a long time of pains in the chest, cough and a lack of appetite; since three years there has been pain in the abdomen, and constipation; the patient has greatly emaciated recently. Examination gave the following: Infiltration in both apices of the lungs; slight feverishness, high-grade stricture of the rectum; five centimeters (two inches about) beyond the entrance of the rectum seemed entirely occluded. On careful search a small opening was found near the posterior wall in which not more than the point of the finger could be inserted. The mucosa itself was perfectly smooth and soft. No nodules or ulcers appeared. The stricture seemed to be caused by a cicatrix, the edge of which was sharp and smooth. With some trouble it was possible to introduce a medium soft male catheter alongside of the finger as a guide. A quantity of stinking fluid feces was discharged and some solid crumbs, and much more of these came away by flushing beyond the stricture. This procedure was frequently repeated for fourteen days and gave momentary relief, but there was no hope of dilating permanently in this way, for the stricture became constantly stronger and tighter and the introduction of the instrument more difficult, the patient complaining more and more and running down rapidly. An operation was indicated and a surgeon in consultation urged division of the stricture.

"Then Dr. P. decided to make a trial with thiosinamine and began with injecting the above-named solution into the gluteal muscles. The first injection was somewhat painful but for a moment only, while all subsequent ones were perfectly painless and without any reactions, so that the further injections could quite readily be made in the same place. The result far exceeded all expectations. After the fifth injection the catheter could be introduced easily and painlessly without the finger as a guide. After the eighth injection a small tube could be used instead of the catheter and the introduction of it with the finger as a guide was accomplished very easily. For the first time then after a long time spontaneous fecal evacuations took place. It was found that two more strictures, less pronounced, and some ulcerations existed above the first stricture. The stricture, it must be mentioned, was perfectly smooth. The injections continued to be painless, and the patient could not express wonderment enough at the results, and laughed at her previous anxiety. Four weeks after the first injection of thiosinamine normal conditions of the rectum presented and the injections were discontinued. The patient evacuated her stools normally and without pain, and that permanently. On the course of the tuberculosis the injections had no influence whatever. The patient bore a living child and unfortunately died fourteen days later of acute miliary tuberculosis.

"Dr. Pollak treated other patients with injections of the same solution for rheumatism and neuritis and always without pain or reaction. In all these the results were good, but he does not give their histories, thinking the one he detailed perfectly sufficient, and this one deserves well enough to be tested by others in similar cases."

Fibrolysin is a double compound of thiosinamine and sodium salicylate. It has the advantage of quick absorption and freedom from pain and irritation when injected subcutaneously. Herschell speaks quite favorably of it, comparing the effects with Bier's passive hyperemia. In moderate doses the action is elective to pathologic connective tissue, though Lange showed that in toxic doses it induced anasarca.

A writer in the *Clinic* says that his uses of thiosinamine by the mouth were invariably disappointing. He finds it only valuable when used hypodermically. He recommends a half grain twice a week, gradually increased to three times a week if necessary. Profuse diuresis always follows its use. The appetite improves and the weight increases. Skin eruptions disappear, cardiac lesions

improve, a hemic murmur disappearing after three months' treatment. In another case a mitral lesion improved markedly. He found thiosinamine useful in keloid and other cicatricial growths, corneal opacities, lupus vulgaris and lupus erythematosus, glandular enlargements, non-specific and non-tubercular, psoriasis, and urethral stricture. Deformities from burns soften to an astonishing degree.

Mendel declared the site of injection immaterial. Plesch, who obtained success in treating Dupuytren's contraction, injected as closely as possible to the contracted tissue. Urbantschitsch favors intravenous injections as giving speedier results. He chose the larger veins to avoid thrombosis. A peculiar taste and odor is almost immediately perceived after the injection, or the technic is at fault. These occur later after subcutaneous and intramuscular injections. Most operators prefer injections into the gluteal region. Sometimes there is burning after the injection, and this may last for hours. The skin may become yellowish or inflamed, or urticaria appear. Painless nodules sometimes form, subsiding slowly. Severe headache and debility may follow for a day. Debility of the limbs, insomnia, nausea, premature menstrual flow, toothache, and fever up to 104° F., have been reported as rare sequences. Waugh noted marked symptoms of heart-failure after injections of five grains, though a Gram has been advised as a single dose in Germany.

Merck mentions as contraindications the existence of valuable supporting cicatrices, active inflammation (which is aggravated by this drug), and latent tuberculosis; arteriosclerosis in the aged, when it may cause congestion, and otorrhea present or recently stopped.

Weisselberg found fibrolysin superior to thiosinamine in esophageal stricture. Thirty-nine injections were given.

Coombe, after a year's study, reported good results in pyloric strictures and in adhesions by bands, laryngeal stenosis, cardiac stenosis, cirrhosis and ascites, and in cerebral sclerosis. Planta cured an extensive scar from a burn with twenty-five injections on alternate days. The patient was a child of five years.

Waelsch cured a plastic induration of the penis; Woltke one of chronic synovitis; Boseek one of myositis ossificans.

Grunert found thiosinamine of use in eye cases, lupoid scars, and post-neuritic atrophy. The improvement was not maintained if the remedy was discontinued too soon. Massage of the scar should always follow the injection.

Bruno also made a favorable report of this agent in eye cases, Brinitzer in scleroderma; Salfield in chronic polyarthrites and arthritis deformans. Kratzer employed it successfully on a horse with fibrous tendinitis.

Lang succeeded in a case of urethral stricture of 53 years' standing. Castellani reported excellent results in the treatment of elephantiasis by the hypodermic injection of fibrolysin, combined with the use of rubber bandages in cases where the skin was verrucose. If the skin was smooth the rubber bandage was not advocated. In one case the patient, who had suffered for twelve years, received 62 injections; at the end of which the circumference of the ankle had been reduced from 23 1-2 inches to 9 inches, the calf from 25 1-2 inches to 12 inches.

Renan found a solution of one part of thiosinamine in 25 of sterilized distilled water, or of normal salt solution, practically painless when injected under the skin of the abdomen. The menstruum must be cold and prepared in a sterilized vessel. The solution is slightly opalescent. Each injection contains 20 centigrams of thiosinamine. Merck suggests a solution of 10 percent strength in four parts of freshly boiled and filtered distilled water, and one part of glycerin. By the mouth the usual dose is 1-2 to 1 grain, three times daily, in tablet or capsules. Injections are given two or three times a week. Unna employs soaps, plasters and ointments of 5 to 20 percent.

When administered by the mouth the result is not satisfactory. Little effect should be expected within three months of the steady administration. The writer failed to secure satisfactory results in one case of chronic synovitis of the knee.

Tyrode's very elaborate experimental study of this drug led him to these conclusions: Thiosinamine undoubtedly produces a profound effect upon the general metabolism when given in sufficient doses. Although the decrease in appetite and later the refusal of food are important factors in the weight, yet the latter is decreased before there is much falling off in the appetite and coincidentally the urea in the urine increases markedly as long as the kidneys are able to secrete. This coincident increase of urea and loss of weight would suggest an augmented katabolism of proteids. Likewise the very general fatty degeneration found after such a short time as six days suggests that the destructive action on the protoplasm of cells is very rapid.

"This, however, does not seem to be specific towards connective tissue since the changes were observed chiefly in epithelial cells.

If thiosinamine has the power of dissolving scar tissue, we would rather expect some action on normal connective tissue, which has not been the case. However, a series of experiments which will form the subject of another publication is now being made with a view of studying the effects upon experimental scars. In view of the marked poisonous action upon animals and also of the reported cases of poisoning in man the writer would recommend that in practice thiosinamine be used only with great caution and in very small doses."

A writer in *Die Therapie d. Gegenwart* suggests that by the use of thiosinamine it may be possible to soften the cicatricial formations in the heart resulting from rheumatism. Three cases were treated by hypodermic injection. A good solution is thiosinamine ten parts, glycerin twenty, and water seventy; warm slightly before using. Of this a hypodermic syringeful may be injected every third day. The results are said to have been quite encouraging, and the patient quickly relieved of insomnia and other troublesome symptoms.

Remete reports the result of his use of thiosinamine in twenty cases of urethral stricture. He used the 15 percent alcoholic solution injecting 15 minims into the back twice a week. The injection was quite painful and cocaine was often required to deaden the pain. The results were favorable. It did not dilate the strictures but the strictures became softer so that dilation was much easier.

Lengemann gave this drug for Dupuytren's contraction, which gives a claw-like appearance to the hands. He says the cures have endured for a year. Forty-five injections were made within eight weeks by which time normal flexibility had been restored. He injects the solution where its effects are desired, preceding with cocaine, following with massage, passive movement and dressings saturated with thiosinamine solution.

McCullagh says that this drug exerts a marked beneficial action on ear disease with the formation of new connective tissue. The benefit is due to increased pliability of this tissue, allowing the usual forms of treatment to accomplish their object better. The administration should always be accompanied by mechanical measures. As good results may be obtained by administration by the mouth as hypodermically. Better and more prompt results may be obtained in recent cases. It exerts a beneficial action on aural vertigo. Care should be used in looking for contraindications. Better results may be obtained with it in the relief of tinnitus aurium than with any drug used heretofore.

Summary: This remedy
Softens scar tissues;
Dissolves pathological fibrous tissues;
Softens strictures and so permits the easy passage of sounds or foods;
Promotes the absorption of nodules and cicatricial tissue.
It has a wide field of usefulness in

Scars	Stenoses
Fibrous adhesions	Ankyloses
Fibrous tumors	Lupus
Strictures	Glandular tumors
Tympanic adhesions	Gastric adhesions
Corneal opacities	Keratitis
Parametritis	Keloid
Locomotor ataxia	Sclerosis
Pyloric obstruction	Elephantiasis
Dupuytren's contraction	Choroiditis

Deafness due to sclerotic processes in the middle ear.

VERATRINE

Standard granule—gr. 1-134, Gm. .0005.

Of the veratrum group veratrum viride has secured the strongest hold upon the medical profession, whose confidence in it has not been shaken by adverse reports, the introduction of German synthetic antipyretics, or even the dreadful accusations of "eclecticism" and "homeopathy." The alkaloidal representative of the green veratrum is generally assumed to be veratrine. We propose to examine this question and ascertain whether this substance really represents veratrum viride therapeutically; and if not, whether either of the other bodies extracted from this group of plants more nearly represents its desirable qualities. For the galenic preparations of veratrum viride are no exceptions to the rule, that all plant-extracts, tinctures, etc., contain their active principles in uncertain and variable quantities and proportions, and hence are fatally wanting in the scientific precision of their application for the cure of the sick.

Veratrum viride contains a little veratrine, pseudojervine, cevadine and veratralbine, with a good deal of jervine, and rubijervine or veratroidine. To the latter two its effects are mainly attributable. Wood claims there is another alkaloid as yet unrecognized save by its effects.

H. C. Wood, Jr., says that veratrum viride is not a vasodilator, the reduction in blood-pressure being due to slowing of the pulse-rate. The chief constituent, protoveratrine, is a heart stimulant. Thus veratrum is a stimulant rather than sedative. If it does good in eclampsia it is by bleeding the patient into his own vessels.

Cevadilla contains veratrine, sabadine, cevadilline, sabadinine and Wright's veratrine. Of these veratrine alone has been studied carefully. The others have not as yet been shown to possess any other importance than as weakening the official veratrine by their presence in variable proportions.

Merck lists: 1. C. P. crystallized veratrine or cevadine (soluble in alcohol and ether); 2, Veratrine, U. S. P., containing the other cevadilla alkaloids but in too small proportion to affect the dosage; 3, Veratrine amorphous; 4, V. acetate, hydrochlorate, nitrate, sulphate and valerate; 5, Jervine; 6, Sabadilline, $C_{21}H_{27}NO_7$, soluble in alcohol, chloroform and benzole, and in 143 parts boiling water; dose twelve times that of veratrine (Urpav); 7, Sabadilline sulphate, soluble in water or alcohol; 8, Sabadine, $C_{29}H_{51}NO_8$, soluble in water, alcohol or ether, also its salts; 9, Sabadinine, $C_{27}H_{45}NO_8$, soluble in water, alcohol, ether or chloroform; also the hydrochlorate, bisulphate and an amorphous form.

Physiologic Action.—Veratrine, $C_{32}H_{49}NO_9$ ($C_{37}H_{53}NO_{11}$, Bruehl), is quite soluble in hot water and alcohol, slightly in cold water. It is absorbed from the skin, the mucous membranes and the subcutaneous tissues. It is rapidly eliminated by the kidneys, and also by the gastrointestinal mucous membrane, the latter being irritated by its passage. When inhaled, veratrine causes dry, irritative and fatiguing cough. Applied to the nasal mucosa it causes violent and prolonged sneezing. Even a granule containing half a milligram, allowed to dissolve in a child's mouth, has raised vesicles. Applied to the unbroken skin, veratrine does not cause redness, but a sensation of burning and prickling, followed by cold and formication, with anesthesia.

Given in moderate doses by the mouth, veratrine increases the excretion of urine, perspiration and saliva, and if continued or increased causes a sense of warmth in the stomach, with burning, nausea, colic, vomiting and diarrhea. Persons unusually susceptible to its action have bloody stools and vomit. The prickling extends over the entire skin, followed by anesthesia and free sweating. Van Renterghem took 0.0005 Gram every half-hour, for thirty-six hours, without experiencing diarrhea, vomiting or any toxic symptom.

Toxic doses cause dilatation of the pupils.

Veratrine exercises a deleterious effect upon certain protoplasms, in which it resembles quinine (Kuen and Scharrenbroich). The lymphatics are thereby rendered less hospitable to microbes; or perhaps the latter are attacked by the veratrine (Van Renterghem).

Absorbed through the skin, veratrine may cause diuresis instead of purging (Bardsley).

Small doses quicken the pulse and respiration and raise the blood-pressure, but larger or repeated doses reverse all these.

The temperature is lowered from the start. This is the case even when minute doses are administered.

At first the vasomotor centers, the peripheral inhibitory nerves and medullary centers are stimulated, later they are paralyzed (Hare).

Toxic doses cause continued weakening of the heart and respiration, which finally cease almost simultaneously. The pulse becomes slow and irregular, breathing slow and labored. Fibrillary contractions of the muscles are frequent, with convulsions, followed by collapse, unconsciousness and death by respiratory failure (Cushny). The nausea may in part be due to direct irritation of the gastric sensory nerve-ends, but is probably due in the main to central irritation. The salivation may be primary, or due to the nausea. The purging is attributable to action on the intestinal nerves; perspiration to stimulation of the nerve-ends, regulating secretion of the sudoriparous glands (Cushny).

The most marked peculiarity of the action of veratrine, is its effect upon the striated muscular fiber. The contractions are strengthened and continuous, relaxation being so slow that coordination is impaired. The relaxation occupies twenty to thirty times the normal period. If the muscle has been fatigued, veratrine causes marked improvement in its contractions. This effect of veratrine is in turn removed by fatigue, or by severe cold or heat; while moderate heat increases or prolongs the effect of the drug (Cushny). Thus, the febrile temperature alters the action of veratrine (Brunton). The heat generated by exercise is increased by veratrine. Both the irritability and the absolute strength of the muscles are increased by veratrine. In the frog, the muscle is finally paralyzed, but in man the respiratory failure occurs long before this is due. This action is peripheric, as it occurs in muscles that have been excised. It is attributed to an increase in the katabolism in the muscular cells (Cushny).

If veratrine is applied directly to the peripheral nerves, their irritability is abolished (Waller).

The ventricular muscular apparatus in frogs is affected like the striated muscles, the auricular fibers much less. The ventricular systole is at first strengthened and prolonged, then the period of contraction is lengthened until one ventricular rhythm corresponds to two of the auricle. Later the contractions become slower and weaker until they cease. In this the action is analogous to that of digitalis. Stimulation of the cardiac inhibitory center slows the heart, lessening its output, the peripheral vessels contracting through central vasomotor stimulation. With larger doses the vagus-ends are paralyzed, its center depressed, the pulse is faster, the tension lowered. No prolongation of the systole is seen, but a slight stimulation, since maximum doses quicken the rhythm even after atropine. Veratrine resembles aconitine as to the circulation, but without stimulating the cardiac muscle (Cushny). The heart stops in diastole (Hare).

Respiration: The action closely resembles that of aconitine, death being by both caused by respiratory paralysis (Cushny).

Central Nervous System: Stimulated as by aconitine, large doses ending in paralysis. The medulla and cord are more affected than the cerebrum, consciousness ending only in death.

Temperature: Lowered by slowing of circulation, unless convulsions are marked, when the temperature is raised.

Veratrine increases reflex excitability (Brunton).

The convulsions of veratrine are always tonic, never clonic or epileptoid. Tetanic spasms are excited by the slightest touch or breath of air (Hare).

Veratrine lessens oxidation somewhat (Brunton).

The peculiar prickling caused by veratrine is felt in the fingers, toes and joints; that of aconitine in the tongue (Brunton). It stimulates the nerves of ordinary sensation and the pulmonary branches of the vagus; the slow pulse caused by it being lessened or abolished by section of the vagi. Stimulation of the vasomotor center is shown by the rise of blood-pressure, ceasing on section of the cord below the medulla; though subsidiary centers exist in the cord itself. Small doses stimulate the cardiac muscle, causing increased energy of contraction, the pulse remaining the same or slower. Larger doses induce a following stage of peristaltic action, and stoppage in either systole or diastole (Brunton).

The effect of veratrine is weakened when it is passed through the liver (Sollmann).

In chronic poisoning the patient becomes weak and thin, with bloody diarrhea, insomnia and delirium (Sollmann).

OTHER VERATRUM ALKALOIDS

Jervine is soluble in alcohol only. It causes sluggishness, progressive muscular weakness and lessened reflexes, violent general tremors, ending in convulsions, with violent motion but loss of power; not tetanic, paralysis rapidly supervening; pupils unaffected, no purging or vomiting, profuse salivation, no local irritation, consciousness continues to the last, death from asphyxia.

The convulsions are cerebral and due to disturbed cerebral circulation. The loss of muscular power is due to spinal depression; the peripheral nerves and muscles are unaffected. It is a direct depressant of the respiratory centers and of the circulation. The pulse at first is slowed; later is faster. The blood-pressure falls from first to last. The action is not affected by vagus section. Direct depression of the heart-muscle or its ganglia is caused by any dose. It depresses the vasomotor centers.

Summary: A powerful depressant of the heart and vasomotor centers, also of the motor spinal and respiratory centers, with little other effect on the body (Wood).

Veratroidine or rubijervine is more irritant than jervine. It usually causes vomiting, sometimes purging, before a fatal dose is absorbed. It does not cause such severe convulsions. Death occurs from paralysis of the respiratory center. It resembles jervine in action on the cerebrum, cord, peripheral nerves and muscles. The circulatory effect is subordinate to that on the respiration. Toxic doses cause an enormous rise in arterial pressure. After section of the vagi, it could not slow the pulse. After intoxication with it, division of the vagi caused enormous rapidity of the pulse. It stimulates cardiac inhibition powerfully, like aconitine. The vasomotor centers are unaffected.

Summary: A powerful respiratory poison, at first slowing the pulse-rate by stimulating the pneumogastrics, but soon losing control of the heart in powerful respiratory paralysis. "The action of veratrum viride is the result of the combined influence of its alkaloids, and as the relative proportions of these differ in different rhizomes, so in the finer details of its physiologic action one specimen of the veratrum viride differs from another" (Wood).

Protoveratrine, $C_{32}H_{51}NO_{11}$, is the principal alkaloid of veratrum album, the others being jervine, rubijervine, pseudojervine and protoveratridine. Locally it causes less sensory irritation than

veratrine, and the anesthesia following is more complete. It does not paralyze the motor nerve-ends in maximum doses. It shortens the muscle-contractions, which are higher, the absolute strength increased, but fatigue follows more quickly than when the drug is not used. It is much more toxic than veratrine, approaching aconitine in strength, while standing between it and veratrine in action. With the rubijervine, it renders white hellebore more irritant to the stomach and bowels than either cevadilla or green hellebore; but this is not uniform, as some cases of poisoning were not marked by severe gastrointestinal action.

Therapeutics.—Both Schmiedeberg and Liebermeister condemn the internal use of veratrine; but Van Renterghem says: "One should not forget that the rise of arterial pressure and the great loss of heat by the skin occasioned by fever, mean something; for this increase of intravascular tension does not necessarily imply an increased oxidation in the tissues, as has been claimed. But it is certain that the state of depression of the circulatory functions occasioned by fever adds a very serious factor to the other causes of fever heat; and that veratrine, prudently administered, suppresses this state and with it its consequences. We possess in our arsenal no medicament as powerful, as sure, as manageable to combat fever, especially acute rheumatism and croupous pneumonia."

We have in this pregnant sentence the key to the uses of veratrine in febrile conditions. "It is especially in acute maladies that its action is powerful. Since its introduction in our hospital practice, there has been no fever or inflammation that we could not direct to resolution" (Burggraeve). "We have always succeeded, grace to it, in producing defervescence, in lowering the most intense fever, in conjuring an imminent inflammation, restraining its development, or mitigating its effects. It has served us with equal success in typhoid fever, puerperal fever, pneumonia, the exanthemata, etc." (Van Renterghem).

A second indication for veratrine is found in its power of causing sedation of the cutaneous sensory nerves. Burggraeve called it "the refresher of the skin," and advised it in erythema, erysipelas, zoster, pemphigus, eczema, ecthyma, urticaria, phlyctenular herpes, febrile aphthæ, boils, carbuncles and malignant pustule; in the latter with the cautery and other indicated remedies. Van Renterghem obtained success from veratrine in pruritic maladies generally. The sedative action of veratrine upon the nervous system renders it suitable in treating neuralgias, the violent pains of rheumatismal ophthalmia, and sciatica. The success following its use in alco-

holic tremor, typhoid convalescence, multiple sclerosis (Feris), chorea (d'Oliveiro, etc.), and tetanus (Harris), may be explained by the action of veratrine on striated muscular fiber. Turnbull and Gintrac gave it in cardiac affections, arthritic and rheumatismal, and for palpitation.

In eclampsia veratrine may well replace the tincture of veratrum viride, which is the most trusted remedy of the profession in this dangerous malady.

Tissot says that in diminishing the torrent of the circulation veratrine decongests the skin and the envelopments of the nerves. Hence its incontestable utility in cutaneous eruptions, and specially in herpes zoster. Its action on the nerves themselves and on the muscles makes it a very active medicament, although somewhat neglected in neuralgias, tremblings, spasms, especially that of tetanus.

Laura says that he has employed veratrine many times in various febrile maladies, without the least inconvenience but with very manifest advantages, especially in cases that resisted aconitine too long, or even aconitine and quinine in remittent forms. Veratrine nearly always rapidly quells these pyrexias in a manner very sweet and without the shadow of an accident. He has used it in every age, even in the most tender infancy, always with success and without inconvenience. By its very efficacious property of profoundly relaxing the sanguine circulation and especially the action of the myocardium and the great arteries, veratrine is useful wherever such relaxation is indicated. Frequently digitalin should be added, as when the heart-action is feeble but rapid, the pulse small and filiform. Veratrine affords the best effects in aneurisms of the aorta, where by relaxing the circulation powerfully it favors the coagulation of the blood in the aneurismal sac. In hypertrophies with excessive passing irritability, with great increase of the cardiac work capable of inducing syncope or collapse, if not arrested in time, and in the nervous palpitations of excessive smokers, Ruatta found veratrine effective. Laura uses it in febrile forms of rheumatism, and others vaunt it in puerperal endometrites and very high post-partum pyrexias, principally in those presenting angiosthenic phenomena. Veratrine gives good results in exaggerated spinal reflexes, epilepsy, eclampsia and puerperal convulsions. It should be useful in cerebrospinal erethisms and even in manias. Here it combats the excessive appetite, opens the elimination, and checks the tendency to excess of blood in the head. All the elements of epilepsy are thus met.

Externally veratrine is employed in the form of an ointment, applied over the course of diseased nerves, with the object of producing analgesia; in various neuralgias, facial, lumbar, spinal and coccygeal.

The dose for internal administration is given as Gram 0.0015 to 0.005 (gr. 1-45—1-12) three times daily, and Gram 0.02 (gr. 1-3) *per diem.* It is little wonder that with such dosage this inestimable remedy has fallen into disuse, and gained the repute of a dangerous weapon. Many persons may be found who cannot take the smallest of the doses named, without unpleasant effects. Except in eclampsia, the dose of Gram 0.0005 (gr. 1-134) should never be exceeded; and this if given every quarter to one hour until the desired effect has been secured, will amply meet every requirement. In every sthenic febrile attack let the bowels be emptied and the alimentary canal rendered aseptic; then administer veratrine, Gram 0.0005, alone or with digitalin and aconitine, or whatever else is indicated. The speedy solubility of veratrine, its rapid elimination, and its power of unlocking every channel of elimination from the body, even when closed by disease that renders ordinary medication perilous, places this remedy in advance of every other. In cirrhotic kidney, when 1-8 grain of morphine or one grain of calomel has caused death, veratrine not only provides for its own elimination but renders the administration of other remedies safer. In true eclampsia alone should the above dose be exceeded. Here the local irritation following the hypodermic application of veratrine must be disregarded, and Gram 0.005 (gr. 1-12) given at once, in diluted alcohol, to powerfully stimulate elimination, and save the brain from the imminent peril threatening it. In other forms of uremia, in diabetic and icteric coma, the same administration should be employed, with due watchfulness. True, the heart's force must be kept up, but that matters little if the brain is overwhelmed by toxins. Veratrine and the normal saline solution meet the need better than any other known remedies.

Given internally in the doses recommended (Gram 0.0005 every quarter to one hour), veratrine should be continued until the first faint intimation of nausea is manifested; then withheld until this has disappeared, or until again indicated by the symptoms. If the stomach develops an idiosyncrasy against veratrine, codeine, Gram 0.005, may be administered with a few doses, provided the pulse and fever show that the antipyretic is still needed. When one has utilized veratrine, in this strictly scientific method of administration, for several years, and become thoroughly familiar

with its properties, its tremendous power, its safety, its perfect manageableness, he can only hear with amazement the condemnation of this alkaloid by men who have good repute as therapeutists.

I have employed veratrine many years as an antipyretic, giving many thousands of the granules. It has proved safe and effective in my hands, safer and more effective than any of the coal-tar series. This has been my experience over the entire range of febrile maladies, in which I have given veratrine whenever the indications showed the sthenic form present, and when there was special need to stimulate the eliminants. I have always used this alkaloid by the common dosimetric method, giving a granule every half hour, hour, two, three or four hours, as the case demanded. I repeat, its efficiency has left nothing to be demanded; and to those who say veratrine is unsafe or ineffective I can only reply that such a statement is conclusive evidence that they have not given this alkaloid a real trial. This statement covers not only my personal experience but the data gathered from an extensive correspondence with very many other active general practicians.

Externally an ointment of veratrine, Gram 0.2—0.5 to 25 Grams of any desired base, may be employed.

"When true sthenic arterial excitement is to be combated in any disease, except gastritis, veratrum viride may be employed as a prompt, thoroughly efficient and at the same time very safe remedy —very safe, since it is almost incapable of producing death in the robust adult. In the early stages of sthenic pneumonia, it offers, we believe, the best known method of reducing the pulse-rate and the temperature, and of lessening the congestion.

"In chronic cardiac diseases it may be used in precisely those cases in which digitalis is contraindicated—i. e., when there is excessive hypertrophy. Over-doses provoke vomiting, so soon and so certainly that it is doubtful whether a robust adult could be killed by a single dose" (Wood).

Veratrum viride is the safest and best circulatory depressant that we have for use in adults. "The physiologic action is to be considered under the effects of its two alkaloids." (Wood.)

Shoemaker recommends veratrine ointments for neuralgia, myalgia, zoster and infantile paralysis; chronic arthritis and acute gouty attacks; in pleurodynia, chronic pleurisy, alopecia circumscripta, chloasma and pediculosis. The officinal ointment is two or more times too strong.

Shoemaker advises veratrum viride in aneurism, exophthalmic goiter, early stages of pneumonia and acute visceral congestions;

in acute hemorrhage and mania, in plethora, in typhoid only with hyperpyrexia and active delirium, in tonsillitis, and to moderate traumatic abdominal inflammations. Phillips gave it for obstinate priapism.

Ringer says it is given for congestive headaches at the menstrual period. He applied the ointment for sick headache, when accompanied or followed by tenderness of the skin.

Synergists.—Aconitine as a defervescent, antiphlogistic and antineuralgic. Cicutine, curarine and digitalin, as to the action on striated muscle fiber, on the motor nerve-ends and on the heart-muscle. Quinine and strychnine for the action upon protoplasm. Colchicine has a similar action on the sensory nerve-ends, but in other respects departs too widely to be ranged in the same class.

Antagonists.—The strychnine group against the respiratory and vasomotor paralysis, the debility and vital depression. Codeine sedates the gastric irritability, lowers topical irritation, and renders veratrine better tolerated.

Chemical antidotes: Tannic acid, iodine, potassium iodide.

Physiologic antidotes: Stimulants, coffee, heat, rest.

Turnbull found the ointment sometimes relieved rheumatic joints; he also applied it over ailing hearts, with rapid irregular pulse, hurried breathing, much lividity and dropsy, palpitation and inability to lie down. Here it acts as a diuretic.

Hare says that the safety of veratrum viride lies in the fact that it excites free vomiting and purging, long before the heart or lung paralysis is reached.

VERBENIN

Standard granule—gr. 1-5, Gm. .0012.

Verbenin is an extract from Verbena hastata, the garden verbena. The root of the wild verbena is the part used.

Felter and Lloyd pronounce verbena tonic, emetic, expectorant and sudorific. In small doses it relieves gastric irritation. Like other diaphoretics it has proved useful in intermittents, and to break up colds and restore menstruation when stopped as a result of taking cold. As a tonic it is useful in debility, anorexia, and in convalescence from febrile affections. It has also been recommended in scrofula, visceral obstructions, gravel, and for worms.

Other species of verbena are said to possess similar properties, though in a less degree. Agnus castus, a European member of the Verbenaceæ, is considered galactagog and emmenagog, and is also

believed to possess the rather contradictory property of subduing the sexual passion. It has also been suggested as a remedy for impotence and for sexual melancholia; possibly may be useful in sexual irritability and nervousness or melancholia, or mild dementia. Castus indicus has been given for venomous bites and stings, and in very small doses for giddiness and salivation.

Dr. H. D. Fair some years ago announced in *The Alkaloidal Clinic* that verbena had proved remarkably effective as a remedy for epilepsy. Subsequently Prof. G. H. French found that the plant possessed some repute among the laity as a remedy for this malady, and tried it with success in some cases. Since that time the extract, verbenin, has been extensively tested, and in a number of cases with success. The writer has given it to a number of epileptics, and is satisfied that there is remedial value in it. Some cases have gone months without convulsions while taking verbenin, and in one case where the spasms occurred at least once a month, a year has elapsed without any convulsions. But in other cases the remedy has had little or no effect. And as yet it has not been ascertained just what verbenin does, how it acts in epilepsy, what cases are amenable to its influence, or in fact what effect it exerts on the bodily functions. Verbena has been recommended as a remedy for intestinal worms. Possibly in some cases a vermifuge or vermicide action may be exerted, as Prof. French at first believed he had found the cause of epilepsy in an intestinal parasite, the larva of a botfly. But it has not yet been shown that epilepsy is due in any great proportion of cases to this or to any parasites, though some cases undoubtedly are. Nor has it been shown that verbenin possesses any action on these parasites.

The whole question deserves investigation. At present we must rest content with the knowledge that verbenin ranks among the drugs that exert an influence over epilepsy, restraining the convulsive tendency better than any other remedy except the bromides in many cases, and without the destructive effects of the latter upon the digestion and the nervous system.

J. M. French, of Massachusetts, says: The older authorities classed it as a tonic, emetic, expectorant, and sudorific, and recommended it as useful in intermittent fevers, colds, obstructed menstruation, and in cases of debility and anorexia occurring during convalescence from acute diseases. They also consider it of value in scrofula, visceral obstructions, and worms.

Dr. J. M. Scudder says that it relieves irritation of the stomach and intestinal canal, and promotes digestion and secretion.

Dr. E. W. Paine states that it has been used with good results in rheumatism, gout and piles.

Dr. E. Day, of Illinois, advocates its use for the cure of intermittent and remittent fevers, and also for the opium habit.

Dr. John W. Fyfe considers that it is specifically indicated in many cases of epilepsy, obstructed menstruation, and acute catarrhal conditions.

Dr. S. M. Griffen advocates the use of verbena as a specific in ivy poisoning; and his claims are corroborated by Dr. Charles Lloyd.

Dr. Henry G. Piffard recommends the plant for alopecia, used locally; while internally he uses it for swollen glands, and in severe headaches with sharp, ringing pains.

Felter and Lloyd describe it as tonic, emetic, expectorant, and sudorific in small doses relieving gastric irritation, and like other diaphoretics useful in intermittents, and to break up colds and restore menstruation when stopped as the result of taking cold.

Its action is said to resemble that of passiflora, and it is indicated in states of nervous tension, mental exhaustion, and insomnia, acting as a soporific, antispasmodic, and sedative. These properties differ widely from those for which it was used by the herbalists —so widely, indeed, as to suggest the question as to whether verbena may not be another of the many drugs whose reputation depends more upon the lively imagination of the user, than upon any important property of the drug itself.

It was the use of the drug in epilepsy which first drew my attention to it, and led me to give it a trial. I did this in the belief that any drug or other agent which holds out any hope, be it ever so small, in the treatment of this intractable disease, is worthy of careful consideration and trial. My present experience with it, however, is limited to two cases, and I cannot claim that it is of any value except as it is added to the wider experience of others.

The questions which I proposed to myself were these: (1) Is verbena of any value in the treatment of epilepsy? (2) If so, is it curative or only palliative? (3) How does it produce its effects, and to what class of cases is it applicable? In other words, what are its indications?

Case 1.—On Nov. 7, 1902, I was called to see a woman of 60, who had been subject to attacks of epilepsy since the age of puberty, though for the most of the time the attacks had not been either very frequent or very severe. She was a woman of good heredity and excellent habits, a widow in comfortable circum-

stances. As a general thing she enjoyed fairly good health in other respects; but for some months previous to my first visit, she had suffered from attacks of more than the usual frequency and severity, and these had produced a greater disturbance of the nervous system than usual and had led her to seek relief by placing herself in the hands of a well-known and competent specialist in nervous diseases in the city of Boston, who gave her the compound bromide treatment.

This method has proven, we know, distinctly beneficial in some cases, but was decidedly injurious in hers. It soon became evident that the effect of the bromides upon her nervous system was very unfavorable. She suffered from the paroxysms with greater frequency than ever before, her nervous symptoms became more marked and uncontrollable, her mind was blurred and confused, and she suffered from headache, backache, derangement of the stomach and intestines, and partial suppression of urine.

It was under these conditions that I was called to see her. I spent two or three weeks in studying the case, and in trying the usual remedies, none of which seemed to benefit her. I therefore resolved to make a trial of this new remedy. On Nov. 25, I began giving her verbenin, using the 1-5-grain tablets, each of which represented eight grains of the crude drug. Of these I gave her at first one before each meal, or three tablets a day; and increased by one tablet a day, until she was taking eighteen tablets a day.

I also regulated her diet quite strictly, limiting the amount of food to the needs of the system, and directing her to avoid nitrogenous food, not wholly but largely. I also ordered her to avoid the use of salt as a condiment, substituting therefor sodium bromide. It soon became evident that even this small amount of bromide was injurious to her, and thereafter she did without salt or any substitute as a condiment, but I did not require her to have her food especially prepared without salt, but allowed her to partake of food from the common table. The change was distinctly beneficial to her, and she has ever since continued the practice. The bowels were kept active by means of a laxative diet so far as possible, and then by the use of cascara tablets. Elimination by the kidneys was promoted by the use of lithia tablets, one in half a glass of water two or three times a day as needed. Moderate exercise was encouraged, but all violent exertion, either of body or mind, was strictly forbidden. Other remedies were used as needed for special symptoms, but this was the dominant treatment. The patient had more than the usual intelligence, and gave me her full and hearty

cooperation in the endeavor to cope with and overcome the serious symptoms which mark this disease.

On February 11, 1903, she had two light attacks. From that time until the Christmas holidays of 1904, a period of about twenty-two months, she was entirely free from the attacks, and her general health was greatly improved. The confusion of mind, the nervous weakness, the annoying headache, backache, and muscular weakness, had entirely disappeared, and the kidneys and bowels were acting properly, so I felt encouraged.

But alas! after all this time, came a reminder of the oft-learned lesson, that while temporary improvement in a case of epilepsy is not uncommon, its permanent cure is almost unheard of. At the Christmas season she was engaged in church work, making preparation for celebrating the glad day. As chairman of a committee of ladies, she was subject to much responsibility and nervous strain—and the result was disastrous. I say the result, and yet who can tell? It may be that the outcome would have been the same if she had not been subject to these untoward circumstances. However that may have been, she did under these circumstances have several not very severe epileptic attacks, and became very much discouraged. This made the matter still worse, and I was under the necessity of casting about to find something to take the place of verbenin. This I finally found in specific solanum, which she began taking about the first of March, and continued for one month only. During this time she became worse than at any time during my treatment of her, and about the close of the month had one of the worst attacks she ever had, in which she fell, and sustained severe injury. Her head became dizzy, her mind confused, and all the worst symptoms recurred.

So there seemed nothing to do but to go back to verbenin, which evidently agreed with her better than anything else that had been tried. She has now been taking this for about six months, and during the first three she had several returns of the attacks, though none of them were as severe as those she had while taking solanum. For the last three months she has been free from them, and has steadily improved. I am therefore obliged, in summing up her case, to say that there has been no cure, and that the present outlook promises only palliation. There was, however, a great improvement lasting nearly two years, and it is evident that the remedy does exercise a considerable degree of control over the nervous system, and a more favorable influence in preventing the convulsions than any other drug or agent which has been tried in her case.

Case 2.—September 12, 1904, I began treating a young lady of 22, who had suffered from frequent epileptic attacks since she was twelve years of age. She was always a delicate child, and suffered from rachitis in early childhood. Bowels always loose, approaching diarrhea. No apparent connection between the menstrual function or the sexual organs and the epileptic attacks. Nor was it evident that they depended upon overeating or derangement of the digestive organs, though it was admitted that she sometimes had an inordinate appetite. No indication of eyestrain. The kidneys acted properly, and the urine was normal. In short, I discovered nothing to point out the cause of reflex irritation, except the possibility of seat-worms, from which she had at times suffered, though but slightly. She also had stomach worms when a child, but was not known to have had any since. Soon after she had her first attack she was taken to the Children's Hospital in Boston, and was there given a careful and thorough examination, with only negative results. Heredity—one aunt had epilepsy. She seemed bright, her head was clear, and did not ache much. She had taken much medicine of many physicians, and had last been using some kind of a bromide mixture, which seemed to have a favorable effect to some degree. The last time before I saw her, she went nine days without an attack, which was considered doing very well.

I gave her the same general directions as to diet and exercise as in the previous case, and began at once with the verbenin in increasing doses, adding the intestinal antiseptic tablet, one after each meal.

She continued this treatment for about three weeks, during which she had at least twice as many attacks as usual, and more severe. Most of the time she had two in one day, which was unusual for her. On the whole she grew decidedly worse, and I could only advise the discontinuance of the verbenin, and a return to the bromides. I further advised that she be treated for seat-worms, and this brought to light a few, but was not given soon enough or followed up long enough to settle the question of their influence in the causation of the epilepsy. She then passed out of my care, and I do not know her subsequent history.

Here then are two cases of epilepsy, with the same general lines of treatment, but quite dissimilar results. What conclusions shall we draw?

I cannot persuade myself that the entire arrest of the convulsions and the coincident general improvement, in the first case, was a mere coincidence, having no relation to the treatment, even

though the results proved to be but temporary. Neither could it have been the result of any form of suggestion; for my encouragement was even less than had been given her by her previous physician, while his treatment resulted in positive injury. In the second case, there was not only failure to benefit, but evident retrogression; which may, however, have been due simply to the withdrawal of the bromides which she had previously been taking.

Putting my own cases alongside those of other observers, I am prepared to suggest the following tentative conclusions as my contribution to the therapy of verbenin in epilepsy:

1. Verbenin is of great value in some cases of epilepsy while in others it is of no value whatever, and may be even injurious.

2. At the best, verbenin is palliative rather than curative—not a remedy *for* epilepsy, but a remedy *in* some cases of epilepsy. None the less it is of value, and well worth further study.

3. As to the indications for its use, I would suggest that it is of value chiefly in those cases which are characterized by cerebral anemia rather than congestion, and which consequently are not benefited by the bromides, but rather the reverse.

The dose of verbenin has not yet been fixed. The writer has advised gr. ss four times a day as a beginning adult dose, adding one daily dose of the same size whenever a convulsion occurs. The average effective dose has been ten grains a day, but some have risen to gr. 20 a day, without any symptoms occurring that could discommode the patient. But no scientific study of verbenin has been made, not even to ascertain its effects upon the excretion of uric acid.

VIBURNIN

Standard granule—gr. 1-6, Gm. .01.

Viburnin is a concentration from Viburnum prunifolium, the black haw or sloe, a native plant of the honeysuckle family. The bark contains two resins, one of which has also received the name of viburnin.

Felter and Lloyd say that large doses cause vomiting. It has been termed nervine, antispasmodic, tonic, astringent, diuretic and alterative.

As an astringent it has been used in diarrheas and dysenteries. Useful in jaundice, chionanthus is better. It relieves palpitations, sympathetic, occurring near the menstrual periods. It is of great utility as a uterine tonic. It restores normal innervation, improves

the circulation, and corrects impaired nutrition of the genital apparatus of women. In the hyperesthetic irritable uterus of very nervous women, or those overworked; in general weakness with feebleness of the uterine functions; dysmenorrhea with deficient menstrual flow; uterine colic, lumbar and bearing down pains, it is efficient. Uterine congestion and chronic metritis, spasmodic dysmenorrhea with excessive flow, malarial menorrhagia, uterine hemorrhage near the menopause, and anemic amenorrhea, are quite markedly influenced by viburnum. Muscular cramps during pregnancy are relieved by it. It is almost specific for cramps in the legs, occurring especially at night. It is the most reliable and prompt agent in the materia medica to check threatened abortion, if given before the membranes are broken.

In habitual abortion small doses should be administered for a long time before the expected occurrence. Phares who introduced viburnum claimed that it would completely neutralize the effects of gossypium when the latter had been taken to cause abortion. In postpartum hemorrhage it is less effective than ergot or cinnamon. It assists in reducing the subinvoluted womb. Viburnum has been utilized for various neuroses, chorea, hysteria, hysteroepilepsy, *petit mal*, and paralysis agitans. It is said to be of value in sterility, spermatorrhea, ovarian irritation, and to control false pains and after-pains is almost equal to macrotin.

Howe employed black haw for dysmenorrhea, leucorrhea, pelvic discomforts and chlorosis, and the debility of the second climacteric. For the user of alcohol his cordial allayed the gnawing in the stomach and the pharyngeal irritation.

Specific Indications.—Uterine irritability and hyperesthesia; threatened abortion; uterine colic, dysmenorrhea with deficient menses, severe lumbar and bearing down pains, cramp-like expulsive menstrual pains; intermittent painful contractions of the pelvic tissues; after-pains and false pains of pregnancy; obstinate hiccough.

Viburnin is one of the native plant-remedies that came like a revelation upon that part of the medical profession that had had little or no experience with the therapeutic treasures of our own land. Like veratrum and many others its introduction was under commercial influences, and yet it has won a large place in the practice of the profession. Its chief field is as a preventive of abortion, and here its influence has been well established. It cannot stop an abortion that has already occurred; nor should it be relied upon to the exclusion of accessory treatment, such as rest in bed, the

avoidance of excitement and the quieting of apprehension, etc. The writer has employed viburnin and potassium bromide each in many cases, and considers the effects of the former better and more effective in every respect.

The dose of viburnin to stop a threatened abortion is from half to one grain, repeated every half hour till effect. The recumbent position must be rigidly maintained; the patient being forbidden to rise even to evacuate the bowels or bladder. After the pains have stopped the remedy should be continued at longer intervals, and generally for months or till the end of preganncy in doses of a grain three times a day.

XANTHOXYLIN

Standard granule—gr. 1-6, Gm. .01.

Xanthoxylin is a concentration from Xanthoxylum fraxineum or Americanum, the prickly ash. An alkaloid has been found in the bark, closely resembling berberine and probably identical with it. This alkaloid has been identified in some xanthoxylum barks from South America. The other alkaloids and other principles in prickly ash have not been studied.

Felter and Lloyd find in prickly ash many virtues. It acts upon the secretions, the nervous and circulatory systems. It has remarkable powers as a sialagog, causes warmth in the stomach and promotes the flow of gastric and intestinal secretions. The bile and pancreatic action is also stimulated, the urine increased. The pulse is a little hastened, the skin acts abundantly. It is especially a stimulant of the sweat glands and the mucous secretions.

It is also emmenagog and carminative, and the berries are antiseptic. It has been given for rheumatic complaints with phytolacca, as an eliminant for debilitated patients; but the cases described are really myalgic—lumbago, torticollis and muscular rheumatism. In toothache it is useful when there is dull pain from peridentitis. As an eliminant it is useful in syphilis and scrofula; in small and frequent doses. It has been employed as a local remedy in glottic paralysis, neuralgias and paretic conditions of the larynx and pharynx. This points to glosso-pharyngeal paralysis, but we doubt the efficacy of any remedy here. But in pharyngitis and post-nasal catarrhs with dry glazed mucous surfaces it probably does good. As a gastrointestinal tonic xanthoxylum is of use in atonic dyspepsia, gastric catarrh, costiveness, flatulence, jaundice from biliary catarrh or from malaria, spasm of the bowels, colic,

cholera infantum and cholera morbus. It is useful after dysenteries, and as a remedy for epidemic dysenteries. King used the berries for Asiatic cholera. He valued it highly in atonic diarrheas and typhoid conditions, and for the tympanites of choleraic maladies. With diuretics and tonics it has good repute in dropsies, malaria and functional dysmenorrhea.

As a nerve stimulant it is given for all forms of nervous prostration, hemiplegia, locomotor ataxia and all varieties of vital depression. It relieves pains down the front of the thighs, after-pains with dorsal or sacral pains, neuralgic pains in anemic and delicate persons. By overcoming capillary stasis it sends to the surface the rashes of the eruptive fevers, especially if retrocedent.

Specific Indications.—In small doses, for hypersecretion from debility and mucous relaxation; in large doses for nerve atony, capillary engorgement in exanthemata, sluggish circulation, tympanites, gastrointestinal torpor with deficient secretion; dry mucosa of mouth and fauces with glazed glossy surfaces, flatulent colic, Asiatic cholera, uterine cramps and neuralgia; for painful bowel troubles the berries are preferred to the bark.

While the eclectics make a distinction between the uses of the bark and those of the berries, they give no data as to a difference in chemistry, nor do their accounts seem to show why there should be the difference in application. They term the bark stimulant, tonic, alterative and sialagog, while the berries are stimulant, carminative and antispasmodic, acting specially on mucous tissues. The bark is also said to be especially stimulant to the mucous surfaces. If there is any difference it would seem likely that the berries contain a carminative volatile oil in addition to the special stimulant of mucous secretion which is present in both parts of the plant. And to the latter the specific virtues of xanthoxylin are to be attributed. An agent that will stimulate the mucous secretions throughout the body, without nauseating or depressing like emetine or lobelin, is of considerable interest, and should receive numerous applications. It should be a good addition to prescriptions for habitual constipation when costiveness is a feature, and for the whole line of dry catarrhs. If the principle to which this effect is due can be isolated it might prove useful as a local application in nasal catarrhs of this description.

The dose of xanthoxylin is gr. 1-6 every one to two hours, until the effect is manifest, then less frequently. In chronic cases and for costiveness the dose may be placed at a grain four times a day.

YOHIMBINE

Standard granule—gr. 1-12, Gm. .005.

Yohimbine is an alkaloid, $C_{23}H_{49}N_2O_4$. For rabbits the toxic dose is Gram 0.011 intravenously and Gram 0.053 subcutaneously, per kilogram of body-weight. In frogs it inhibits the heart-action, stopping it in diastole, and paralyzes respiration. The vascular tension is relaxed, the pulse-rate being unaffected. In warm-blooded animals small doses cause unrest, excitement and erections, and large doses cause violent spasms, followed by weakness. It paralyzes the motor centers but not the sensory. Oberwarth showed that the aphrodisiac effects are exerted upon the nerve centers. Bartholow suggests that it may prove useful in albuminuria, by substitution.

As reports accumulate upon the use of yohimbine as an aphrodisiac, its true action is becoming defined and its place in therapeutics fixed. The hydrochlorate is the form in which it is best prescribed, as this is comparatively stable, while pure yohimbine alkaloid is altered by the action of air and light.

Yohimbine is sharply differentiated in its effects. It produces hyperemia of the penis and testicles, in a short time after its exhibition. Repeated for a considerable period, no ill-effects were noted, and no degenerative change could be discovered on post-mortem. In locomotor ataxia and other organic disease no ill effect followed the use of this drug. In neurasthenia and nervous erethism marked benefit was obtained from it. Sometimes the benefit was immediate, but in other cases several weeks were required to obtain the good effects. Pains have been taken to exclude the influence of suggestion. Berger gave three times the usual dose, or .015 Grams thrice daily, in some cases, before the desired action was manifested. No ill effects followed these doses. He suggests that if the benefit wears off the drug should be discontinued for a time; but those who have tested the drug most carefully do not agree with this.

Yohimbine is a local anesthetic, less toxic than cocaine. Full doses cause vertigo and other symptoms referable to cerebral vasodilation. In animals the sexual stimulation is produced at once. Why this does not always occur in man is not yet explained satisfactorily.

In one case it seemed to stir up an old orchitis. In another, a lady normal anatomically but devoid of sexual desire or sensation, the only effect from yohimbine was prolongation of menstruation.

Daels concludes from experiments made on animals that yohimbine simply increases the menstrual flow in females, without any effect of stimulating the sexual function or appetite. In some instances, however, an increase in sexuality has been noted, associated sometimes with serious psychic disturbances. These must be regarded as evidences of a toxic action, and guarded against in the dosage.

Yohimbine may be given by the stomach or hypodermically. For hypodermic use the hydrochlorate must be dissolved in boiling water. This solution will keep for a few weeks, and longer if a drop of chloroform is added. It is advised to give the tablets containing Gram .005 each, three times a day, for six weeks or more, rather than to give larger doses.

It is quite evident from the reports that yohimbine is strictly limited in aphrodisiac effect to the stimulation of erection and producing congestion of the testes; with, inferentially, an increase in their secretion, though this is not stated by any paper on this drug we have yet read. But it is absolutely devoid of any power to arouse or increase sexual desire. It is not a drug to aid the seducer. When desire is present but erection imperfect or absent, yohimbine is the remedy indicated. This condition as caused by dilation of the penile veins, seems unknown to the Germans, and some of the failures recorded from yohimbine may be due to this condition. If so it is quite explicable that an agent relaxing vascular tension would not give relief.

Dr. J. Rutter Williamson records three cases in which he administered yohimbine, with the desired result. One of his patients was a young man who, through nervousness and want of erectile power, had failed to consummate the marriage act during the entire two years of his wedded life. Medication with strychnine, caffeine, damiana, cantharides and capsicum had proved fruitless. Three 10-milligramme doses of yohimbine brought about a restoration to normal function.

The two other cases were almost identical with that above described, except that the impotence had been of briefer duration and responded to doses of half the amount (5 milligrammes).

The high price at which yohimbine is held ($1.00 a grain) will limit its use for a time; but if it acquires a permanent place in therapeutics the price will undoubtedly subside. At the best that place can not be an important one unless new uses are discovered. **Cornin** is a better tonic to the erectile tissues, requiring longer to develope activity but more enduring.

ZINC CYANIDE

Standard granules—gr. 1-67, Gm. .001; gr. 1-6, Gm. .01.

Therapeutically the cyanide of zinc represents hydrocyanic acid and the preparations depending on this potent agent for their therapeutic value. Not one of these is trustworthy, uniform or safe in its applications. The writer has purchased the dilute acid, U. S. P., from the greatest manufacturers in the country and found it absolutely inert, in teaspoonful doses. He has tried to use potassium cyanide, bitter oil of almonds, etc., and the liquor known as noyau, the latter being the most satisfactory of all; but he had to give up the use of these agents, as none of them was sufficiently uniform in activity to be fairly safe. Zinc cyanide has proved all that could be asked in these respects, uniformly active and not subject to decomposition like the potassium salt.

Zinc cyanide is odorless and tasteless, insoluble in water and in alcohol, soluble in caustic alkalies and in ammonia. Strong mineral acids decompose it, setting free the hydrocyanic acid.

Henning employed this salt as a substitute for hydrocyanic acid, and found it satisfactory. It also exerted a vermifuge effect. In the nervous affection termed cramp of the stomach he gave gr. 1-4 with magnesia and cinnamon every four hours. It has been recommended in chorea, epilepsy, and other neuroses. In neuralgia, especially of the fifth nerve, it appears to be of value; and in neuroses of the heart with arrhythmia, pain and palpitation, doses of gr. 1-4 every hour or two have been advised.

The double cyanide of zinc and potassium has the advantage of being freely soluble in water. The dose is the same as of the preceding.

In the stomach, however, zinc cyanide is decomposed by the acid of the gastric juice, setting free the hydrocyanic acid. Given in too large doses the chloride of zinc formed will irritate the stomach. The effects of glonoin so closely resemble those of the cyanides that they should be considered synergistic.

Hydrocyanic acid occurs in the seeds of the apple, cherry, prune, plum, peach and apricot; and especially in the bitter almond.

Kirschwasser and maraschino, as well as noyau, contain this acid. Laurel water and wild cherry contain the acid in very small quantities. The action of the acid and of its single salts is identical, but the double cyanides are mostly inert—or at least harmless.

Physiologic Action.—Hydrocyanic acid is a protoplasmic poison, first stimulating and then paralyzing the central nervous

system. Cushny places the fatal dose for man at gr. 1 to 1 1-2 of the pure acid. It acts with the greatest rapidity. After very large doses there may be no symptoms—the animal falls with a slight convulsion or a scream, and death ensues in a few moments from paralysis of the heart and respiration. In small doses it has a bitter acrid burning taste, with salivation, followed by numbness in the mouth and throat. Warmth in the stomach is followed by nausea, vomiting, mental confusion, headache, dyspnea, slow pulse, and general muscular weakness. The pupils dilate widely and the eyeballs protrude. Unconsciousness follows, then convulsions, passing into paralysis, the bladder and bowels acting involuntarily. Respiration weakens and ceases, the heart continuing to beat for some time longer. The action seems to develop in the medulla and basal parts of the brain rather than in the cortex. Some local anesthesia is caused.

Small doses quicken and deepen respiration. The pulse is slowed by stimulation of inhibition, and the pressure rises from vasoconstrictor central stimulation. Paralysis of both follows from increased doses, but as the cardiac muscle is directly affected the pulse remains slow. The movements of the stomach are lessened; the temperature rises a little after small doses, falls fast after toxic doses (Cushny).

Death may be instantaneous, patient convulsed, cyanotic, eyes staring, teeth clenched, bloody froth on lips; milder cases show dyspnea, slow pulse, disturbed brain, convulsions, shrinking, dilated pupils, vomiting, forcible passing of urine and feces, priapism, ejaculation, asphyxia, collapse, death.

Geppert found that prussic acid lessened the absorption of oxygen by the tissues, and less carbonic acid was excreted. Oxyhemoglobin not being reduced in the capillaries, the venous blood was as red as the arterial. The acid is rapidly decomposed in the blood, so that the symptoms are of brief duration. The acid is changed to sulphocyanides in the tissues, and is partly excreted through the kidneys in that form. Part undergoes other changes, whose nature is unknown.

Therapeutics.—Zinc cyanide may be prescribed to meet symptoms resulting from increased sensibility of the cerebrospinal system, and excitement of the heart. It may soothe intense pains, calm exalted sensibility, and prevent reflex spasms. In laryngitis and acute respiratory inflammations Van Renterghem associates it with aconitine, digitalin and strychnine; in spasmodic and painful affections of the air passages and abdominal organs, in convulsive

cough and that of phthisis, cardialgia, colic and vomiting; and in the chronic nervous maladies, epilepsy, chorea, hypochondria and hysteria, he finds the field for this agent. In organic diseases of the heart and great vessels it calms over-action; applied locally it relieves pain and itching.

In acute cases of children it is wise to give it cautiously at first, a granule gr. 1-67 every hour or two, until the susceptibility is ascertained. But to adults this dose may be given every quarter-hour, or doubled. In cardialgias we may add strychnine or hyoscyamine, after having emptied the bowels; in heart cases join to digitalin or the arsenates, and care for the doses, which may be a granule or two four or five times a day; in the neuroses add veratrine, cicutine, arsenates, atropine, strychnine, bromides, or other remedies as may be indicated.

It is always better to use the smaller dose and multiply the doses, as the drug is quickly decomposed or eliminated; and thus the irritation of the stomach is avoided. In many of its uses glonoin has perhaps replaced the cyanides, but the latter relieves irritative cough and nausea, which the former does not do. In the cough of phthisis especially, the use of zinc cyanide enables us to dispense with opiates for a long time. Here the action of the zinc on the stomach is usually beneficial as it acts as an antiseptic, and this action is needed.

ZINC OXIDE

Standard granule—gr. 1-6, Gm. .01.

Zinc oxide being insoluble is less apt to irritate the stomach than the chloride, or even the sulphate of zinc. In small doses the oxide soothes irritation of the stomach, allays nausea, checks diarrhea, and tends to restore a chronically catarrhal mucous membrane to its normal state. A specialist of very great experience stated to the writer that he considered the curative effects of zinc oxide superior to those of all the other metallic salts in use.

Zinc is excreted in the bile and the urine, and by the lining of the stomach and bowels. Its continued action or exposure to its fumes, as in those working with it, results in a condition of chronic poisoning, characterized by malaise, weakness, vague pains, rigors, fast pulse, cough, soreness in the thorax, and headache. Profuse sweating occurs, followed by sleep. These attacks recur frequently.

Therapeutics.—Zinc oxide has been given for epilepsy, chorea, hysteria and a variety of neuroses, with considerable bene-

fit. It is one of the most reliable remedies for gastric ulcer, and especially as following the oxide of silver when the latter must be discontinued to avoid argyria. It has been advised in whooping-cough, catalepsy, neuralgia and gastrodynia. It is decidedly useful in the gastric and nervous symptoms of drunkards, relieving the nausea, tremors, vertigo, insomnia, tinnitus and hallucinations. Taken during the evening it prevents night-sweats. Felter and Lloyd give the following specific indications; Nervous dyspepsia, broad tongue and full abdomen, gastric ulcer, chronic gastritis with free mucous secretion; night-sweats.

The book doses of zinc oxide are too large. It is best given in doses of gr. 1-6 to 1 every hour or two, stopping when there is the first sign of irritation. It is the least irritant, most effective and safest preparation of zinc for the effects of that metal.

ZINC PHOSPHIDE

Standard granules—gr. 1-67, Gm. .001; gr. 1-6, Gm. .01.

The action of zinc phosphide being identical with that of phosphorus, we will consider here the latter element, looking upon the salt named as the best available means of securing the therapeutic effects of phosphorus.

Physiologic and Toxic Actions.—Large doses of phosphorus have been swallowed without harm resulting, because its insolubility prevents its absorption. But if absorbed it causes toxic symptoms in very small doses. Two grains have proved fatal to man. Phosphorus vapor is absorbed by the lungs and causes poisoning in factories. It is absorbed and exerts its effects as phosphorus itself.

No effect is manifested from toxic doses for some hours; when pain and uneasiness are felt in the stomach with nausea, eructations of garlicky odor, and vomiting of matters with the same odor, which are phosphorescent. There may be vomiting of bile, and diarrhea. These symptoms may last some days or cease after the stomach has been washed out. But they are apt to recur, with jaundice and pain extending to the liver and over the abdomen. The vomitus may be bloody. There is pronounced debility, the pulse weak, liver enlarged, urine albuminous, with ecchymoses and hemorrhages from the mucosa, collapse and coma. Convulsions and delirium may precede death. Death may occur at any stage. Recovery may ensue even from the second stage, provided the treatment is instituted before fatal lesions have been inflicted.

Exposure to the fumes of phosphorus causes necrosis of the lower jaw. This is apt to start with a carious tooth. It may also cause chronic poisoning, with cachexia, jaundice, anemia and albuminuria; followed by chronic enteritis, diarrhea, bronchitis and fragility of the bones.

Fat globules appear in the cells of the liver, kidney, glands of the stomach and bowels, and the muscular fibers of the heart, stomach, intestine, small arteries and sometimes in the striated muscles. Cirrhosis appears in the stomach, liver and kidneys.

When doses too small to set up the above symptoms are taken, changes occur in the growing bones. Dense bone is deposited in cartilage instead of cancellous, and already formed cancellous bone is absorbed. The medullary cavity is thus enlarged.

When death occurs early in poisoning from phosphorus it is due to a direct action upon the cardiac muscle. The blood does not clot as readily as usual. Small doses increase the number of red cells, but not the hemoglobin, and lessen the number of white cells. Fatty degeneration of the epithelium explains the gastrointestinal symptoms. The enlargement of the liver is due to fat. The renal epithelium becomes fatty, and fatty casts and globules appear in the urine, with blood and hemoglobin. At first the excretion of urine is increased, later it becomes scanty and may cease. The excretion of nitrogen is lessened by the vomiting but later increases, even if fasting. Ammonia increases much more than urea. Sarcolactic acid is found in large amount; the uric acid is little altered, the extractives increased; tyrosin, leucin, albumin and peptone appear. Harnack found some substances not peptones though closely related. The chlorides are much reduced, the phosphates increased, as are the sulphates, and bile may be present. All these alterations point to a grave derangement of metabolism. The alkalinity of the blood is reduced. The glycogen of the liver is remarkably reduced. The two factors conclusively shown to exist in phosphorus poisoning are fatty degeneration and lessened oxidation in the tissues.

Phosphorus has little effect on microorganisms, or on the digestive ferments. It is partly oxidized in the body, partly excreted by the lungs, and partly by the kidneys in various combinations.

Phosphorus poisoning calls first for thorough evacuation of the stomach, as the poison is absorbed slowly. Oil of turpentine forms with phosphorus compounds not very toxic, and may aid in its oxidation; hence is used as an antidote. The benefits are doubtful. Sulphate of copper is also used as an emetic and as forming

with it an insoluble compound. In the secondary stage alkalies are given to neutralize the excess of acid. The necrosis is to be treated surgically.

Therapeutics.—Phosphorus has proved useful in rickets and in osteomalacia. This has led to its use for caries and necrosis, and for ununited fractures. Phosphorus has been largely employed as a remedy for nervous debility and exhaustion, neurasthenia, insomnia, the results of over mental work; also for the more serious consequences of such excesses, softening of the brain or paresis, with very little demonstrable benefit. As a general tonic its use betrays ignorance or culpable rashness on the part of the prescriber. It is too dangerous a drug to be employed as a substitute for iron, quinine and the hypophosphites. In many neurotic maladies it is given with the hope rather than the expectation of benefit; such as all forms of paralysis, locomotor ataxia and the whole line of convulsive affections.

In neuralgia its use is better based: In dealing with pure neuroses there is something in taking the malady by storm, as it were; and a course of treatment instituted vigorously at the beginning will succeed in making a favorable impression when the same remedies given timidly till the system has become accustomed to them will fail. To such a case as an inveterate neuralgia give zinc phosphide gr. 1-6, strychnine arsenate gr. 1-30, the arsenates of iron and quinine gr. 1-6 each, with atropine valerate gr. 1-134; all together every four hours, and within two days the force of the malady will be broken, and milder doses will complete the cure. When any neurosis is traceable to sexual, alcoholic or other excesses, phosphorus may prove beneficial. Senile degenerations may be temporarily benefited by this potent agent, but in impotence the writer has never seen any but ill results. There may be a momentary stimulation of the sexual function but it is followed by quicker exhaustion. Phosphorus will not make an old man young.

It has been advised in melancholy, dementia, various forms of mental failure and aberrations, but not even occasional success has resulted from the writer's use of the drug here. Scudder advised it through the whole line of chronic and atonic vesical and seminal affections, but its value has not been demonstrated.

In the low stages of fevers, typhoid, pneumonia and malaria, phosphorus has been recommended as a stimulant; but just now strychnine is preferred. Still there may be a place here for phosphorus. The use of modern methods in these and other fevers has rendered such emergencies almost obsolete.

The use of phosphorus for fatty degeneration of the liver, and for malignant jaundice is no more to be condemned as "homeopathic" than its undoubted use in rickets and osteomalacia.

Felter and Lloyd give as specific indications: Nervous exhaustion, atony, vesical and prostatic irritation with mucoid discharges; fulness and dragging in the perineum; weariness in legs; mucoid rectal discharges; low muttering delirium in low fevers with involuntary discharges; chronic bronchial and pulmonary affections with heat, dryness, hacking cough, and difficult expectoration of mucopurulent or sanguineous sputa; rusty sputa; pulmonary hyperemia; pinkish face with staring eyes; expressionless pasty tongue; insufficiency of the internal recti of the eye; sexual debility.

The writer has employed zinc phosphide for many years in every case of herpes zoster applying for treatment, and has never found a case that resisted the remedy. He gives to an adult, gr. 1-6 an hour before each meal, and within two days the attack is under control. If this malady is due to degeneration of the roots of the affected nerves, there is reason for the use of the same remedy in other maladies, dependent on that condition; and in this also we have not been disappointed. Localized neuroses in general come under this description and for them we would urge a trial of this remedy.

The full adult dose of zinc phosphide we would place at gr. 1-6 four times a day, given as far as possible from the meals to avoid the development of phosphureted hydrogen. The difficulties encountered in administering phosphorus are so numerous that it seems advisable to go over the whole list for which it has been advised with the more manageable and safer, yet efficient, zinc phosphide.

ZINC SULPHOCARBOLATE

Standard granules and tablets—gr. 1-6, Gm. .01; gr. 1, Gm. .06; gr. 2, Gm. .15; gr. 5, Gm. .3.

The sulphocarbolates were introduced many years ago, as intestinal disinfectants, but fell into disuse before they were fairly tried. Two arguments were adduced against them—that it was impossible to render the alimentary canal free from germs; and that these agents being soluble they were absorbed from the stomach and did not get down to the intestine where their effects were most desired.

In regard to the first objection, it is well to ask whether it is really necessary to destroy every living inhabitant of the alimentary

canal in order to do any good? There are many ways by which the great benefits derived from the intestinal antiseptics may be explained. They may destroy a portion of the microorganisms, or prevent their multiplication, or neutralize the toxins produced by them, or prevent their inroads upon the mucous tissues, or render the tissues more resistant, or interfere with the attacks of the ordinary putrefactive bacteria that follow in the wake of specific organisms like the typhoid bacilli and break down the weakened structures. In fact, we do not know so much of the life history and the operations of the various bacteria that we can deny the usefulness of such an agent simply because it does not do some one thing that we have set up arbitrarily as a test of its value. The only test worth serious consideration is that of clinical trial; and the question is not whether the remedy does this or that, but how we can best explain the phenomena which follow its administration. This question has been wholly ignored by the opponents of the practice of intestinal antisepsis.

An insoluble agent is inert until it is in solution. Then it is no longer insoluble. Many attempts have been made to devise means of getting remedies past the stomach to be dissolved only when they reach the small bowel, but the solvent powers of the gastric juice are exerted even over keratin. This is an *a priori* consideration—we have as yet seen no attempt at demonstration of the assertion that agents soluble in the stomach will not disinfect the intestine. We are therefore again reduced to the necessity of relying on the phenomena observed clinically, and here we find that the administration of the sulphocarbolates in efficient doses is invariably followed by a cessation of abnormal odor of the stools. Why this should be, if the soluble antiseptics have no action in the intestine, we leave those who believe that dogma to explain.

The writer has possibly administered more of the sulphocarbolate of zinc than any other man living; and he has not observed any effects from it except those exerted in the alimentary canal. If impure, or given in too large doses or too concentrated form, it irritates the stomach and may even cause vomiting. But the chemically pure salt has been given many times in doses of ten grains each, and up to two drams in twenty-four hours, without any such effects. There are conditions of the stomach when many agents not ordinarily irritant will provoke nausea or cause soreness. Sometimes a granule of veratrine in half a glass of water will give rise to a sense of warmth or tenderness that will outline the stomach accurately. A five-grain tablet of potassium bromide swallowed

whole, caused a brother physician to roll on the floor in agony; and yet this is not considered spêcially irritant. It is wise to give the sulphocarbolates in solution or trituration with abundance of diluent.

Dr. A. H. Simonton called attention to the diuretic action of the sulphocarbolates, which he asserted that he had noticed in his own case. In order to test the matter, we secured a sample of urine on February 8, which was examined in our laboratory. Another sample from the same case was taken on February 14, after the patient had taken four intestinal antiseptic (three sulphocarbolates) tablets every two hours, from 7 a. m. to 7 p. m. on the preceding day.

The laboratory report is as follows: First sample: Specific gravity, 1027; amount passed in twenty-four hours, 37 oz.; total solids in twenty-four hours, 989 gr.; acidity, 75.7 percent; urea in twenty-four hours, 21 Gm. (normal 33); uric acid, 1.8 Gm. (normal 0.6); sodium chloride, 18.6 Gm. (normal 10.15); chlorine, 11.2 Gm. (normal 7.8); phosphoric acid, 2.53 (normal 3.16); sulphuric acid, 2.53 (normal 2.01); albumin, indican and sugar absent; bile present.

The sample taken February 14, after taking the intestinal antiseptic tablets, gave the following results: Amount in twenty-four hours, 98 oz.: specific gravity, 1020; total solids, 2156 gr.; total acidity, 40.7 percent; total urea, 33 Gm.; total uric acid, 1.4 Gm.; total sodium chloride, 38 Gm.; total chlorine, 23 Gm.; total phosphoric acid, 3.82; total sulphuric acid, 5.58; albumin and sugar absent; bile and indican present.

This would indicate an enormous increase in the excretion of solids of the urine, and a still greater increase in the excretion of water. The presence of indican in the second sample is an anomaly. While the dose of the sulphocarbolates was larger than would be likely to be taken by any average person, it must be remembered that the subject here was unusually large, his weight being 274 pounds.

Therapeutics.—Typhoid Fever. In all cases it is essential to first completely empty the bowels. It is useless to try to disinfect the intestine if there is present the mechanical obstacle of masses of feces into which the disinfectant cannot penetrate. Give a dose or two of calomel and then a saline laxative; and when the bowels have been cleared out well begin with zinc sulphocarbolate, giving from 2 1-2 to 5 grains every two hours until the stools are devoid of all abnormal odor. After this half the above doses, or even less,

will suffice to keep the stools deodorized, and this will disinfect them sufficiently to secure all the advantages of the method. The gastric and intestinal symptoms subside as the stools become odorless; the fever drops a degree or more, the aching, delirium and other nervous phenomena are alleviated, and the whole aspect of the case has changed for the better. If employed early enough many cases are shortened or aborted, so that the physician who begins to employ this method soon has trouble with his diagnoses.

Cholera Infantum.—In all cases when the child's stools begin to be offensive treatment analogous to that of typhoid fever should be instituted. Give calomel in very small doses, or rhubarb, and empty the alimentary canal; then begin with zinc sulphocarbolate, gr. 1-6 to 2 every hour according to the gravity of the case, and continue until the stools are disinfected. If choleraic symptoms are present begin at once with the zinc. It is best given with bismuth and saccharated pepsin if there is nausea or vomiting—enough of each to well dilute the zinc.

Fevers.—In all fevers, essential and symptomatic, the above method of emptying and disinfecting the bowels will result in an amelioration of the symptoms amounting to thirty or forty percent. There is no febrile disease in which a large part of the symptoms, the discomfort and danger, is not due to absorption of toxic matters from the alimentary canal—at least we are sure our readers will admit that such absorption cannot be of any advantage to the patient. This seems to have been better comprehended by the physicians of half a century ago than it is today; excepting in the malarial sections, where the necessity of having the bowels clear and clean is generally admitted and acted upon.

Phthisis.—It was a lesson the writer has never forgotten, when he first applied to a consumptive the principle of clearing out the bowel and disinfecting it. The same fall in the fever occurred as in typhoid fever, the other symptoms were ameliorated, and the appetite, hitherto wanting, became voracious. This one measure produced in the patient more improvement than the most ingeniously devised treatment had previously accomplished.

In fermentive dyspepsias, and all cases where the stools are malodorous, this agent will prove promptly effective. It is an admirable remedy for children, who very frequently need something of the sort. While clearing out the bowels will do good, it needs but a trial to convince anyone of the greater benefit coming from the disinfection. The alkaline syrup of rhubarb makes an excellent excipient for the sulphocarbolates.

When there is acidity, or when the zinc proves irritating even if given properly extended, the sulphocarbolate of soda is useful. It is not as antiseptic as the zinc, and should be given in double the doses recommended for the latter.

In dealing with scrofulous children, in the peculiar diarrhea of rickets, and for consumptives who are having night-sweats, the sulphocarbolate of lime may be used. It is about the same strength as the soda salt. In fact, whenever the reconstructive effects of lime are indicated, this is the sulphocarbolate of choice. It may be given with the hypophosphite or other salts of lime.

ZINC VALERATE

Standard granule—gr. 1-6, Gm. .01.

Zinc valerate presents one of the best agents from which to secure the remedial values of valerian. The dose is small, the acid active, and through the whole line of its action the zinc favors the effects of the valerian.

Felter and Lloyd mention this agent as an antispasmodic, used in neuralgias, especially spinal and of the fifth nerve; also in chorea, epilepsy, neuralgic and nervous headaches, hysteria, sciatica, ovaralgia, and angina pectoris. The specific indications are: Colic, reflex from ovarian or uterine disease, headache, paleness, dizziness, sleeplessness, anemia.

Many cases of insomnia are over-treated. Due to nervousness, they are quickly relieved by a few granules of zinc valerate. Nervous unrest, worry, irritability, crossness, fidgets, even well-founded grief such as that from the death of a friend, are relieved by valerian. Or at least it enables the afflicted one to bear the grief with equanimity, to hold the emotions under decorous control. Probably all forms of disturbed nervous and emotional equilibrium are tranquilized by this remedy.

The writer has found the insomnia of typhoid fever yield to zinc valerate in very moderate doses. Even that occurring during the withdrawal of morphine from a habitue is notably benefited by valerian. Sexual excitement is regulated by this agent, controlled but not weakened, and for nymphomania, satyriasis, spermatorrhea, and the erethism so common after abuse of the sexual functions, there is no better agent for restoring the strength and the control at the same time. This remedy is as useful for one sex as for the other. If the patient has been in the habit of taking the powerful stimulants or hypnotics much larger doses of the valerian

preparations are necessary. The ataxic state sometimes developing in the course of a typhoid fever is controlled by this agent, although camphor or some one of the aromatic antispasmodics is generally advisable also. These feeble remedies in this perilous condition manifest a therapeutic power far more decided than one would expect who relied upon them in hysteric affections for suggestive powers alone. A full dose may be given at once, or small doses quite frequently, until the nervous equilibrium has been restored.

The dose of zinc valerate for an adult is gr. 1-6 repeated every quarter-hour till effect. Overdoses simply irritate through the zinc.

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	cardiac	convallamarin	326
		strychnine	634
	catarrhal	aconitine	28
	spasmodic	emetine	378
Ataxia, locomotor		acetanilid	27
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		cannabis indica	239
		chromium sulphate	272
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		physostigmine	523
	pain	pilocarpine	531
		santonin	591
		zinc phosphide	671
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Atony, general		apocynin	68
		cornin	331
		corydalin	332
		iron	457
		lobelin	479
	capillary	capsicin	251
	connective tissue	bebeerine	146
		berberine	152
		xanthoxylin	662
	genitourinary	arbutin	77
	intestinal	aloin	55
		apocynin	68
	nervous	cypripedin	340
	uterine	anemonin	59
	vascular	apocynin	68
		collinsonin	313
		hydrastine	417
Atrophy		iridin	455
		iron arsenate	461
		nuclein	511
Atropine			120
Atropine arsenate			120
Autotoxemia		calcidin	216
		cerium oxalate	260
		cicutine	275
		copper arsenite	327
		creosote	334
		juglandin	463
		podophyllin	547
		resorcin	575
		rhein	576
		salicylic acid	582
		zinc sulphocarbolate	674
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Backache		æsculin	49

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Bad blood		iridin	455
		rumicin	581
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Baptisin			139
Baptitoxine			139
Barium chloride			142
Barosmin			145
Bebeerine			146
Bedsores		echinacea	370
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Belladonna			120
Benzaconine			28
Benzoic acid			147
Berberine			152
Bhang			237
Bicycle heart		cactin	184
		collinsonin	313
		convallamarin	326
Bile:	deficiency	boldine	173
Bilein			155
Biliary calculi (see calculi hepatic)			
Biliousness		benzoic acid	147
		boldine	173
		bryonin	182
		copper arsenite	330
		iridin	455
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		sodium succinate	603
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Black eye		anemonin	59
Bladder affections		anemonin	59
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		benzoic acid	147
	catarrh	barosmin	145
		benzoates	150
	irritable	atropine	134
		barosmin	145
		cantharidin	244
		eupurpurin	396
		hyoscine	429
		hyoscyamine	447
		populin	550
		senecin	602
	leaky	collinsonin	313
		eupurpurin	396
	pain	codeine	297
	paralysis	ergotin	382
		rhus tox	580
		strychnine	628
	relaxation	chimaphilin	269
	spasm	cannabis indica	244
		gelseminine	400
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Blepharospasm		cicutine	279
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		arsenic sulphide	110
		atropine	134
		calcium sulphide	224
		echinacea	370
		ergotin	382
		intestinal antiseptic	392
		iron	460
		potassium permanganate	551
		resorcin	575
		rhus tox	577
		zinc sulphocarbolate	674
Boldine			173
Bowel:	spasm	atropine	134
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		benzoic acid	147
		caffeine	202
		digitalin	362
		glonoin	406
		gold	408
		zinc phosphide	671
	congestion	aconitine	28
		atropine	134
		caffeine	202
		colchicine	311
		croton oil	336
		echinacea	370
		jalapin	462
		nickel bromide	509
	diseases	bryonin	179
	hyperemia	aloin	55
		benzoic acid	147
		codeine	297
		colocynthin	318
		croton oil	335
		elaterin	373
		gelseminine	398
	inflammation	atropine	120
	softening	cannabis indica	237
		gold	408
		lecithin	470
		nuclein	513
		zinc phosphide	671
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Breast (see mastitis).			
Breath, bad		colchicine	311
		juglandin	463
		zinc sulphocarbolate	674
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Bronchial glands enlarged		calcidin	213
		phytolaccin	526
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Bronchitis		acetanilid	27
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		anemonin	59
		antimony arsenate	64
		apomorphine	71
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Bronchitis		aspidospermine	115
		atropine	134
		bryonin	179
		cannabis indica	240
		caulophyllin	259
		cetrarin	262
		cicutine	280
		collinsonin	313
		creosote	335
		iodoform	453
		nuclein	512
		scillitin	593
		stillingin	625
	acute	camphor monobromide	232
		codeine	300
		cubebin	337
		emetine	378
		eupurpurin	396
		menthol	491
		narceine	505
		nickel bromide	510
		pilocarpine	531
		veratrine	651
	capillary	apomorphine	71
		calcidin	215
		emetine	378
		potassium bichromate	550
		rhus tox	577
		sanguinarine	589
		scillitin	593
	chronic	arsenic	85
		benzoic acid	148
		calcidin	215
		cerium oxalate	261
		euonymin	394
		helenin	413
		macrotin	484
	fetid	benzoic acid	148
		calcium sulphide	218
		creosote	334
	spasmodic	aspidospermine	115
		cicutine	275
		codeine	300
		hyoscyamine	447
		lobelin	479
Bronchopneumonia		calcidin	215
		helenin	413
		iodoform	453
		nuclein	513
Bronchorrhea		arbutin	77
		atropine	120
		berberine	152
		calcium sulphocarbolate	674
		codeine	300
		creosote	335
		hydrastine	417
		menthol	491
		resorcin	575
		salicin	582
		strychnine	628
		zinc oxide	668
Brucine			176

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Bruises		apiol	65
		calcium sulphide	218
Bryonin			179
Bubo		arsenic iodide	109
		calcidin	213
		calcium sulphide	218
		phytolaccin	526
Buchu			80
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		codeine	299
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Cachexias		alnuin	54
		arsenic iodide	109
		calcidin	213
		condurangin	320
		cornin	331
		corydalin	332
		iodoform	453
		iridin	455
		iron	459
		juglandin	463
		lecithin	470
		manganese	487
		phytolaccin	526
		populin	550
		rhus tox	577
		stillingin	625
Cactin			184
Caffeine			193
	arsenate		193
	hypodermically		193
	sulphonates		193
Calabarine			521
Calcalith			208
Calcidin			213
Calcium benzoate			150
	carbonate (calcalith)		208
	iodized (calcidin)		213
	sulphide		218
	saturation		218
Calculi		chionanthin	270
		gelseminine	400
	hepatic	atropine	134
		boldine	173
		cannabis indica	239
		dioscorein	367
		leptandrin	477
		salicin	582
		sodium succinate	603
	renal	atropine	134
		cannabis indica	239
		chimaphilin	269
		eupurpurin	396
	uratic and phosphatic	benzoic acid	147
Camphor monobromide			230

Disease	*Phase*	*Remedy*	*Page*
Cancer		aconitine	28
		arsenic	96, 99
		cannabis indica	239, 240
		cantharidin	248
		chelidonin	263
		cicutine	279
		condurangin	320
		gold	409
		hydrastinine	425
		iodoform	452
		nuclein	513
	gastric	cerium oxalate	261
		chelidonin	263
	hepatic	atropine	134
		codeine	300
	inoperable	cicutine	275
	intestinal	chelidonin	263
		condurangin	320
	mammary	echinacea	370
		hydrastine	417
	pain	aconitine	28
		cicutine	275
		salicin	586
Cannabis Indica			237
Cantharidate sodium			244
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Cantharidin oil: Dietrich's			244
Capillary engorgement		aconitine	28
		hamamelin	417
	stimulant	echinacea	370
Capsicin			251
	as a condiment		251
Carbuncle		arsenic sulphide	110
		calcium sulphide	218
		echinacea	370
		nuclein	511
		resorcin	575
		rhus tox	577
Cardiac diseases (see heart)		veratrine	651
Cardialgia		arsenic	85
		atropine	134
		calcidin	213
		cicutine	275
		condurangin	320
Caries		zinc phosphide	671
	dental	cicutine	280
Car sickness		brucine	176
		copper arsenite	327
		emetine	375
		juglandin	463
		menthol	491
		pepsin	520
		rhein	576
		salicylic acid	582
		cascarin	256
Cataract		anemonin	59
		atropine	134
		calcidin	213
Catarrh		aconitine	41
		anemonin	59
		apocynin	68
		calcalith	208

Disease	*Phase*	*Remedy*	*Page*
Catarrh		colchicine	312
		collinsonin	313
		cubebin	338
		phytolaccin	526
	acute	aconitine	41
		atropine	134
		hamamelin	411
	nasal	atropine	134
		camphor monobromide	230
		morphine	495
		pilocarpine	531
		quinine	559
	respiratory	emetine	378
		lobelin	479
		sanguinarine	589
		veratrine	651
		zinc cyanide	667
	atonic	helenin	413
	children's	asclepidin	112
	dry	ammonium benzoate	150
		apomorphine	71
		lobelin	479
		xanthoxylin	662
	duodenal	boldine	173
		copper arsenite	327
		dioscorein	367
		echinacea	370
		emetine	378
		euonymin	395
		iridin	455
		juglandin	463
		sodium succinate	603
	fetid	creosote	334
		resorcin	575
		salicylic acid	582
	gastric	emetine	378
	chronic	capsicin	253
		leptandrin	477
	gastrointestinal	asclepidin	112
		berberine	152
		colchicine	312
		condurangin	320
		eupurpurin	396
		hydrastine	417
		physostigmine	521
		rhein	576
		salicin	582
		strychnine	628
		zinc oxide	668
	genitourinary	arbutin	77
		barosmin	145
		benzoic acid	147
		berberine	152
		chimaphilin	269
		collinsonin	313
		cubebin	338
		rhus tox	577
	hypertrophic	hydrastine	417
	intestinal	physostigmine	523
		quassin	552
	laryngeal	calcidin	213
		sanguinarine	588

Disease	*Phase*	*Remedy*	*Page*
Catarrh	moist	hydrastine	417
	nasal	hydrastine	417
		sanguinarine	588
		xanthoxylin	662
	nasal pharyngeal	calcidin	213
		potassium bichromate	550
	non-febrile	arsenic	85
	of aged	sodium benzoate	151
	pharyngeal	capsicin	253
	respiratory	asclepidin	112
		echinacea	370
		sanguinarine	588
	uterine	arbutin	77
		berberine	152
		calcium sulphide	227
		hamamelin	411
Caulophyllin			257
Cellulitis:	ischiorectal	baptisin	139
Cephaeline			260
Cerebral concussion		ergotin	382
	diseases (see brain)		
	engorgement	hydrastine	417
		rhus tox	577
	hemorrhage (see apoplexy)		
	hyperemia from teething	cypripedin	340
Cerebrospinal fever		aconitine	28
		baptisin	142
		cannabis indica	240
		echinacea	362
		elaterin	374
		ergotin	382
		gelseminine	399
		hyoscine	427
		rhus tox	577
		veratrine	651
Cerium oxalate			260
Cervical glands (see adenitis).			
Cetrarin			262
Cevadilla			645
Chancre (see syphilis)			
Chancroid		hydrastine	417
		iodoform	452
Chapped skin		benzoic acid	149
Chelidonin			262
Chest injury		bryonin	179
	pains	asclepidin	112
		zinc phosphide	671
Chilblains		capsicin	255
		resorcin	575
Chilling from cold		capsicin	255
Chills		atropine	120
		glonoin	404
		pilocarpine	531
	congestive	capsicin	254
		piperine	546
		strychnine	628
	initial febrile	capsicin	254
	nervous	strophanthin	626
Chimaphilin			269
Chionanthin			270
Chloral poisoning		strychnine	628
Chloroform poisoning		glonoin	404

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Chloroform poisoning		strychnine	628
Chlorosis		aloin	55
		caffeine	193
		caulophyllin	259
		cetrarin	262
		iron	458
		lecithin	470
		manganese	484
		nuclein	511
	amenorrheic	aletrin	54
Cholera		arsenic	85
		atropine	134
		capsicin	254
		piperine	546
		strophanthin	626
		strychnine	628
		zinc sulphocarbolate	674
	collapse	arsenic	85
		atropine	134
		capsicin	254
		glonoin	404
		nuclein	511
		strychnine	628
	dry tissues	camphor monobromide	232
	infantum	aconitine	28
		atropine	134
		benzoic acid	149
		bryonin	179
		capsicin	254
		cerium oxalate	260
		copper arsenite	328
		echinacea	370
		emetine	378
		geranin	403
		mercury	492
		nuclein	513
		resorcin	575
		rhein	576
		strychnine	628
		zinc sulphocarbolate	674
	dysenteric	collinsonin	313
		hydrastine	417
	nervous	caffeine valerate	193
		echinacea	370
		zinc valerate	676
	morbus	atropine	134
		calomel	492
		capsicin	254
		cocaine	294
		echinacea	370
		emetine	375
		juglandin	463
		menthol	491
		nuclein	513
		pepsin	520
		resorcin	575
		rhein	576
		rhus tox	577
		strychnine	628
		zinc oxide	668
		zinc sulphocarbolate	674
	pain	dioscorein	367

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Chordee		aconitine	28
		atropine	134
		camphor monobromide	232
		cannabis indica	240
		cantharidin	248
		colchicine	312
		gelseminine	400
		lobelin	479
		veratrine	651
Chorea		acetanilid	27
		aconitine	28
		arsenic	85
		atropine	135
		avenine	138
		barium chloride	142
		bebeerine	146
		camphor monobromide	232
		caulophyllin	258
		cerium oxalate	260
		cicutine	283
		cocaine	294
		collinsonin	313
		copper arsenite	327
		curarine	340
		cypripedin	340
		delphinine	346
		ergotin	382
		gelseminine	400
		hyoscine	429
		hyoscyamine	447
		lobelin	479
		macrotin	484
		nuclein	513
		physostigmine	522
		picrotoxin	529
		scutellarin	602
		strychnine	628
		veratrine	651
		zinc cyanide	667
		zinc oxide	668
		zinc valerate	676
	early menstrual	viburnin	661
	major	barium chloride	142
	with endocarditis	sparteine	621
Chromium sulphate			272
Cicutine			275
Cinchonidine			284
Cinchonine			285
Cirrhosis		boldine	173
		gold	408
	liver	convallamarin	326
		dioscorein	367
		iodoform	453
Cocaine			285
	cantharidate		294
	habit		294
	poisoning		294
Codeine			297
Cohosh: blue			257
Colds		asclepidin	112
		calcidin	213
		camphor monobromide	232

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Colds		capsicin	252
		emetine	375
		eupurpurin	396
		macrotin	484
		pilocarpine	534
		sanguinarine	588
Colchicine			302
Colchicum poisoning			313
Colic		asclepidin	112
		caulophyllin	258
		dioscorein	369
		hyoscyamine	448
		menthol	491
		picrotoxin	529
		piperine	546
		rhein	577
		zinc valerate	676
	bilious	calcidin	213
		dioscorein	369
	flatulent	capsicin	253
		menthol	491
		physostigmine	521
	from worms	bryonin	179
	hepatic	atropine	120
		boldine	173
		chelidonin	264
		codeine	299
		collinsonin	313
		dioscorein	369
		glonoin	405
		hyoscyamine	448
		sodium succinate	604
	of horses	arecoline	83
	infantile	collinsonin	313
		lobelin	479
		menthol	491
	lead	atropine	135
	renal	atropine	135
		hyoscyamine	448
	stercoral	bryonin	179
Colitis: mucous		arsenic	103
Collapse		atropine	135
		camphor monobromide	232
		capsicin	252
		glonoin	405
		strychnine	628
Collinsonin			313
Colocynthin			315
Colon torpor		bryonin	179
Coloproctitis		juglandin	463
Color blindness		santonin	591
Coma		apomorphine	71
		caffeine	201
		capsicin	251
	of jaundice	veratrine	651
Coma vigil		hyoscyamine	447
Condurangin			318
Congestion		aconitine	28
		glonoin	405
		iodoform	453
	cerebral	capsicin	251
	hepatic	leptandrin	477

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Congestion		quinine	559
	hypostatic	cantharidin	244
	passive	digitalin	349
		ergotin	382
	pulmonary	sanguinarine	588
	renal	digitalin	349
Conium			275
Conjunctivitis		aconitine	28
		ergotin	382
		hydrastinine	425
		physostigmine	521
		phytolaccin	526
Connective: atony		berberine	152
Constipation		aloin	55
		anemonin	59
		apocodeine hydrochloride	67
		apocynin	68
		arecoline	85
		atropine	135
		berberine	152
		bryonin	180
		capsicin	254
		cascarin	256
		collinsonin	313
		colocynthin	318
		emetine	379
		euonymin	394
		hydrastine	417
		iridin	455
		jalapin	462
		juglandin	463
		leptandrin	477
		lobelin	478
		menispermine	490
		physostigmine	521
		phytolaccin	526
		podophyllin	547
		podophyllotoxin	547
		rhein	576
		strychnine	637
	chronic	emetine	379
Consumption (see phthisis)			
Contractions		cicutine	275
Contraction:	Dupuytren's	thiosinamine	642
	hour glass	caulophyllin	257
Contracture:	spasmodic	narceine	504
Convalescence		avenine	138
		bebeerine	146
		caffeine	199
		hydrastine	417
		iron	460
		lecithin	470
		populin	550
		quassin	552
Convallamarin			324
Convulsions		aconitine	28
		apomorphine	71
		atropine	135
		benzoic acid	147
		cicutine	280
		curarine	338
		gelseminine	397

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Convulsions		veratrine	651
	epileptic (see epilepsy) (see hysteria)		
	infantile	emetine	378
		lobelin	479
		nickel bromide	509
		rhus tox	577
		scutellarin	601
		veratrine	651
	puerperal (see eclampsia)		
Copper arsenite			327
Coprostasis of insane		hyoscyamine	447
Cornea:	foreign bodies in	cocaine	285
	inflammation	atropine	135
Cornin			331
Corns		arsenic	85
Corydalin			332
Coryza		calcidin	217
		calcium sulphide	218
		camphor monobromide	230
		cocaine	295
		cubebin	337
		gelseminine	400
		salicylic acid	582
Cotarnine			507
Cotoin			333
Costiveness		aloin	55
		jalapin	463
		lobelin	479
Cough		apomorphine	71
		atropine	135
		codeine	300
		hyoscyamine	447
		lobelin	479
		macrotin	484
		morphine	499
		narceine	506
	atonic	eupurpurin	396
	bronchial	rhus tox	579
		stillingin	625
	constant	codeine	300
	convulsive	cicutine	275
		glonoin	404
	croupy	potassium bichromate	550
	dry	asclepidin	112
		calcidin	215
		calcium sulphide	218
		emetine	378
		lobelin	479
		rumicin	581
	hoarse	calcidin	215
		pilocarpine	531
	insufficient	sanguinarine	588
		scillitin	591
	irritative	antimony arsenate	64
		atropine	135
		bryonin	179
		calcidin	215
		emetine	380
		zinc cyanide	667
	laryngeal	bryonin	179
	nervous	butyl-chloral-hydrate	182

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Cough	spasmodic	aspidospermine	115
		camphor monobromide	232
		cannabis indica	239, 244
		codeine	297
		gelseminine	400
		helenin	415
		hyoscyamine	447
	too loose	benzoic acid	147
		berberine	152
	tubercular	iodoform	452
	winter	emetine	378
Cramps:	abdominal	caulophyllin	259
		dioscorein	367
		zinc cyanide	667
	muscular	gelseminine	400
	stomach	hyoscyamine	447
Creosote			334
Crossness		rhein	576
Croton oil			335
Croup		aconitine	28
		antimony arsenate	64
		atropine	120
		calcidin	214
		collinsonin	313
		emetine	380
		lobelin	479
		phytolaccin	526
		pilocarpine	531
		sanguinarine	588
		scillitin	591
		stillingin	625
	membranous	calcidin	213
	spasmodic	aconitine	28
		apomorphine	71
		aspidospermine	118
Crusta lactea		iridin	455
Cubebin			337
Curarine			338
Cyanosis		aspidospermine	119
	neonatorum	glonoin	407
Cypripedin			340
Cystitis		aconitine	28
		apiol	65
		arbutin	77
		asparagin	115
		atropine	120
		barosmin	145
		benzoic acid	149
		cantharidin	248
		caulophyllin	259
		chimaphilin	269
		collinsonin	313
		cubebin	337
		elaterin	373
		gelseminine	402
		salicylic acid	584
		sodium benzoate	151
		veratrine	651
	catheter	arbutin	77
	chronic	boldine	174
	gonorrheal	arbutin	77
		calcium sulphide	218

Disease	*Phase*	*Remedy*	*Page*
Cystorrhea		barosmin	146

D

Dandruff		berberine	152
Deafness		benzoic acid	147
		pilocarpine	531
		thiosinamine	638
Debility		cornin	332
		echinacea	370
		helenin	413
		hydrastine	417
		lecithin	470
		nuclein	513
		strychnine	628
	after fevers	corydalin	332
	from age	capsicin	254
	from indigestion	populin	550
	nervous system	picrotoxin	529
Decay:	premature	lecithin	470
Delirium		aconitine	28
		atropine	135
		bryonin	179
		croton oil	335
	active	gelseminine	400
	of fevers	camphor monobromide	232
		hyoscyamine	447
		nickel bromide	509
		zinc valerate	676
	low muttering	zinc phosphide	671
	maniacal	apomorphine	71
		veratrine	651
	tremens	apomorphine	71
		atropine	135
		camphor monobromide	232
		cannabis indica	239, 244
		capsicin	253
		cicutine	275
		cocaine	294
		digitalin	362
		emetine	378
		hyoscine	429
		hyoscyamine	447
		pilocarpine	543
		scopolamine	600
		scutellarin	601
	typhoid	hyoscyamine	447
Delusions of persecution		delphinine	341
		hyoscyamine	447
Dementia		atropine	135
		baptisin	141
	acute	cannabis indica	239
	chronic	hyoscyamine	447
		strychnine	628
		zinc phosphide	671
Dengue		atropine	135
Dentition ailments		atropine	135
Despondency		caffeine	193
		cocaine	294
		helonin	416
		juglandin	463
Development imperfect		lecithin	470

Disease	*Phase*	*Remedy*	*Page*
Diabetes insipidus		atropine	135
		cantharidin	248
		codeine	300
		ergotin	386
		eupurpurin	396
		hamamelin	412
		helonin	416
		pilocarpine	531
Diabetes mellitus		arbutin	77
		arsenic	98, 99, 100
		cantharidin	248
		cocaine	294
		codeine	300
		creosote	334
		gold	409
		iodoform	453
		iron	460
		lecithin	470
		morphine	499
		nuclein	513
		potassium permanganate	551
		salicylic acid	582
		sodium benzoate	151
	cerebral irritation	cannabis indica	240
	coma	veratrine	651
	itching	cannabis indica	240
	pancreatic	diastase	347
Diarrhea		alnuin	54
		arsenic	85
		atropine	135
		baptisin	139
		caffeine	202
		calcium sulphide	229
		cascarin	257
		cinchonidine	285
		codeine	300
		copper arsenite	329
		cotoin	334
		echinacea	370
		emetine	378
		geranin	403
		hamamelin	412
		iron	460
		juglandin	463
		morphine	499
		narceine	505
		nuclein	513
		piperine	546
		potassium permanganate	551
		resorcin	575
		rhein	576
		zinc oxide	668
		zinc sulphocarbolate	674
	acid	mercury with chalk	491
		sodium sulphocarbolate	624
	atonic	aloin	55
		berberine	153
		brucine	176
		cotoin	334
	bilious	juglandin	463
	burning	iridin	455
	catarrhal	asclepidin	112

Disease	*Phase*	*Remedy*	*Page*
Diarrhea	chronic	cerium oxalate	261
		iron arsenate	461
		salicin	582
		sodium benzoate	151
		strychnine	628
		zinc sulphocarbolate	674
	epidemic	cotoin	333
	fermentative	zinc sulphocarbolate	674
	fetid	juglandin	463
		zinc sulphocarbolate	674
	green	copper arsenite	329
	infantile	berberine	153
		rhein	576
		zinc sulphocarbolate	674
	in hot climates	arecoline	83
		zinc sulphocarbolate	674
	irritative	potassium bichromate	550
	lienteric	arsenic	85
		copper arsenite	326
	morning	rumicin	581
	painful	menthol	491
	passive	capsicin	253
	rickets	calcium sulphocarbolate	674
		cotoin	334
	septic	mercury biniodide	491
	summer	hydrastine	417
		juglandin	463
		rhein	576
		zinc sulphocarbolate	674
	travelers	berberine	153
		rhein	576
	tuberculous	calcium sulphocarbolate	674
		cotoin	334
	typhoid	zinc sulphocarbolate	674
Diastase			347
Digitalein			349
Digitalin			349
Digitaliresin			349
Digitalis:	cumulative		349
Digitonin			349
Digitoxin			349
Dioscorein			367
Diphtheria		aconitine	28
		arsenic	85
		atropine	135
		baptisin	140
		benzoic acid	149
		calcium sulphide	224
		echinacea	370
		hamamelin	411
		hydrastine	417
		mercury	492
		nuclein	514
		pilocarpine	531
		potassium permanganate	551
		resorcin	575
		salicylic acid	584
		sodium benzoate	151
Dipsomania (see alcoholism and delirium tremens)			
Dizziness		aletrin	54
		zinc valerate	676
Dreams:	bad	cannabis indica	240

Disease	*Phase*	*Remedy*	*Page*
Dropsy		aconitine	28
		adonidin	47
		ammonium benzoate	150
		apiol	65
		apocynin	68
		arbutin	77
		asparagin	114
		benzoic acid	148
		bryonin	180
		cactin	188
		caffeine	206, 207
		cannabis indica	244
		caulophyllin	257
		chimaphilin	269
		colocynthin	318
		convallamarin	326
		digitalin	362
		eupurpurin	396
		pilocarpine	534
		scillitin	593
	cardiac	apocynin	68
		mercury	492
	exanthematous	chimaphilin	269
		euonymin	394
	from debility	chimaphilin	269
	hepatic	apocynin	68
		elaterin	374
	malarial	quinine	559
	renal	apocynin	68
		eupurpurin	396
	scarlatinal	apiol	65
		benzoic acid	148
		cantharidin	248
		eupurpurin	396
		pilocarpine	531
Drowning:	to resuscitate	glonoin	404
Drowsiness		baptisin	140
		caffeine	193
Dry mouth		pilocarpine	534
Duboisia			369
Duboisine			369
Dwarfishness		lecithin	468
		nuclein	511
Dysentery		aconitine	28
		asclepidin	112
		baptisin	140
		bryonin	179
		calcium sulphide	229
		cotoin	333
		echinacea	370
		emetine	380
		ergotin	382
		gossypin	410
		iodoform	453
		iridin	455
		juglandin	463
		leptandrin	477
		mercury	492
		morphine	499
		piperine	546
		rhein	576
		sodium benzoate	151

Disease	*Phase*	*Remedy*	*Page*
Dysentery	algid	capsicin	254
	catarrhal	asclepidin	112
	chronic	arbutin	77
		berberine	153
	nervousness of	cannabis indica	240
	relaxed stages	capsicin	254
	severe forms	emetine	380
	tenesmus	atropine	135
		gelseminine	397
	with bad breath	baptisin	140
Dysmenorrhea		acetanilid	27
		aletrin	54
		ammonium chloride	58
		anemonin	59
		apiol	65
		atropine	135
		butyl-chloral-hydrate	183
		caulophyllin	258
		cerium oxalate	260
		collinsonin	313
		corydalin	332
		dioscorein	369
		eupurpurin	396
		glonoin	407
		helonin	417
		iridin	455
		nuclein	514
		picrotoxin	529
		sanguinarine	589
		viburnin	661
	congestive	gelseminine	400
		hydrastinine	424
	membranous	arsenic	85
	neuralgic	apiol	65
	spasmodic	cicutine	284
		senecin	603
Dyspepsia		alnuin	54
		arbutin	77
		arsenic	97, 99
		atropine	135
		bebeerine	146
		berberine	152
		bryonin	180
		caffeine	202
		capsicin	253
		cerium oxalate	262
		chelidonin	264
		chionanthin	271
		cocaine	295
		collinsonin	313
		condurangin	320
		cornin	331
		corydalin	332
		euonymin	394
		hydrastine	417
		iron	459
		juglandin	463
		leptandrin	477
		lobelin	479
		papayotin	518
		pepsin	521
		quassin	557

Disease	*Phase*	*Remedy*	*Page*
Dyspepsia		resorcin	575
		sanguinarine	588
		xanthoxylin	662
		zinc oxide	668
	atonic	aletrin	54
		apocynin	68
		arbutin	77
		berberine	152
		boldine	174
		capsicin	253
		gold	408
		helenin	414
		picrotoxin	529
		strychnine	633
	fermentative	echinacea	371
		zinc sulphocarbolate	674
	fetid	ammonium salicylate	587
	flatulent	emetine	380
		physostigmine	521
	ice water	arsenic	85
		cerium oxalate	261
		hydrastine	417
Dysphagia		cicutine	280
	tubercular	cocaine	295
		iodoform	453
Dyspnea		æsculin	49
		apomorphine	71
		aspidospermine	118
		atropine	135
		benzoic acid	147
		cactin	188
		caffeine	206
		camphor monobromide	232
		convallamarin	324
		glonoin	404
		hyoscyamine	446
		lobelin	479
		lycopin	482
		physostigmine	521
		zinc phosphide	671
	asthmatic	aspidospermine	115
		hyoscine	429
	cardiac	strophanthin	626
		strychnine	628
	gastric	cerium oxalate	261
		xanthoxylin	662
	phthisical	aspidospermine	115
	respiratory	calcidin	215
		physostigmine	521
	uremic	elaterin	373
Dysuria		anemonin	59
		arbutin	77
		atropine	135
		chimaphilin	269
		eupurpurin	396
		gelseminine	400
		hyoscine	429
		hyoscyamine	446

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Earache		aconitine	28

Disease	*Phase*	*Remedy*	*Page*
Earache		anemonin	59
		cicutine	282
	tensive	bryonin	179
Echinacea			370
Eclampsia		atropine	131
		benzoic acid	148
		camphor monobromide	235
		croton oil	335
		ergotin	391
		glonoin	406
		hyoscyamine	449
		lobelin	479
		morphine	503
		pilocarpine	531
		veratrine	650
Eczema		aconitine	28
		alnuin	34
		arsenic	111
		arsenic sulphide	111
		atropine	135
		calcalith	208
		cannabis indica	232
		cantharidin	248
		chelidonin	264
		corydalin	332
		helenin	413
		hydrastine	417
		iron arsenate	460
		juglandin	463
		nuclein	514
		pilocarpine	531
		podophyllin	547
		resorcin	575
		rhus tox	577
		stypticin	508
		zinc phosphide	671
	anal	arsenic	85
	capitis	berberine	152
	chronic	iridin	456
	dry	lobelin	478
	moist	berberine	152
	vulvar	berberine	152
Edema		cactin	188
		chelidonin	264
	glottis	pilocarpine	531
	subretinal	benzoic acid	147
Elaterin			373
Elecampane			413
Elephantiasis		cetrarin	262
		thiosinamine	643
Elimination defective		eupurpurin	396
Emetine			375
Emissions		atropine	135
		camphor monobromide	232
		cantharidin	248
Emphysema		aspidospermine	118
		atropine	135
		camphor monobromide	232
		cicutine	275
		iron	459
		physostigmine	523

Disease	*Phase*	*Remedy*	*Page*
Endocarditis		aconitine	28
		arsenic	96
		bryonin	179
		cactin	184
		hyoscine	427
		lycopin	482
		phytolaccin	526
		strophanthin	626
Endometritis:	catarrhal	helenin	413
	chronic	eupurpurin	396
Enteralgia		aconitine	28
		benzoic acid	147
		cannabis indica	239
		chelidonin	263
		codeine	300
Enteritis		aconitine	28
		cotoin	333
Enuresis		anemonin	59
		arbutin	77
		atropine	135
		cantharidin	248
		ergotin	390
		eupurpurin	396
		santonin	591
	nocturnal	atropine	135
		benzoic acid	147
		strychnine	628
Epididymitis		aconitine	28
		anemonin	59
	gonorrheal	podophyllin	547
Epilepsy		acetanilid	27
		aconitine	28
		adonidin	47
		apomorphine	71
		arsenic	85
		atropine	135
		avenine	138
		camphor monobromide	232
		cannabis indica	240
		cantharidin	248
		caulophyllin	258
		cerium oxalate	260
		cicutine	275
		chromium sulphate	274
		curarine	340
		cypripedin	340
		delphinine	347
		digitalin	349
		duboisine	369
		gelseminine	400
		glonoin	406
		gold	408
		hydrastinine	425
		hyoscyamine	447
		lobelin	479
		nickel bromide	510
		physostigmine	522
		picrotoxin	531
		santonin	591
		solanine	610
		strychnine	628
		verbenin	656

Disease	*Phase*	*Remedy*	*Page*
Epilepsy		zinc cyanide	667
		zinc oxide	668
	anemic nocturnal	picrotoxin	531
	with dropsy	benzoic acid	147
	with vertigo	camphor monobromide	232
Epistaxis		aconitine	28
		benzoic acid	147
		cetrarin	262
		emetine	380
		hydrastinine	425
		stypticin	507
Epithelioma		arsenic	85
		chelidonin	264
		condurangin	318
		picric acid	529
		resorcin	575
		sanguinarine	588
		thiosinamine	638
	uterine	narceine	505
Erections:	weak	cornin	331
		yohimbine	664
Erethism		avenine	139
		bryonin	179
		camphor monobromide	235
		cypripedin	341
		morphine	501
		scutellarin	601
		zinc valerate	676
	nervous	avenine	138
		hyoscyamine	449
	sexual	caulophyllin	257
Ergotin			382
	hypodermically		382
Erotomania		calcium sulphide	218
		salicin	582
		veratrine	651
Erratic pains		viburnin	661
Eructations		berberine	152
		physostigmine	522
Eruptions:	delayed	atropine	135
		helenin	413
Erysipelas		aconitine	28
		atropine	135
		baptisin	141
		benzoic acid	149
		calcium sulphide	226
		echinacea	371
		ergotin	382
		lobelin	479
		picric acid	528
		pilocarpine	534
		resorcin	575
		rhus tox	577
		salicylic acid	582
		sodium benzoate	151
		sparteine	620
		veratrine	650
	asthenic	iron	459
	sthenic	pilocarpine	534
Erythema		atropine	135
		rhus tox	577
		veratrine	650

Disease	*Phase*	*Remedy*	*Page*
Erythema		zinc cyanide	667
Erythrol tetranitrate			394
Esophagismus		atropine	135
Esophagitis		camphor monobromide	230
Esophagus:	stricture	thiosinamine	638
Euonymin			394
Eupurpurin			396
Exanthemata		aconitine	28
		ammonium chloride	58
		asclepidin	112
		avenine	138
		pilocarpine	534
		sodium benzoate	151
Excesses		avenine	138
		lecithin	468
		nuclein	514
		zinc phosphide	671
Excitability:	morbid	cicutine	275
		scutellarin	601
Exhaustion:	febrile	avenine	138
		caffeine valerate	193
		strychnine	628
Exophthalmus		lycopin	482
		calcidin	216
		cannabis indica	240
		digitalin	367
		duboisine	369
		hyoscyamine	448
		iridin	455
		nuclein	514
		quinine	565
		sparteine	621
		strophanthin	627
		veratrine	651
Extremities:	cold	chelidonin	262
Eye affections		atropine	128, 135
		anemonin	59
		pilocarpine	534
	inflammations	arsenic iodide	109
		calcidin	213
		colchicine	311
		gelseminine	397
		iodoform	453
		mercury biniodide	491
		veratrine	651
	burning	rhus tox	577
	injury	physostigmine	523
	nervous strain	butyl-chloral-hydrate	182
		hyoscyamine	447

F

Fainting		aletrin	54
		atropine	135
		brucine	176
		glonoin	404
Fatigue		caffeine	201
		capsicin	251
		cocaine	294
		veratrine	651
	vomiting	phytolaccin	526

Disease	*Phase*	*Remedy*	*Page*
Fecal impaction		codeine	300
		hyoscyamine	447
		strychnine	628
	vomiting	atropine	135
Feet cold		atropine	135
		capsicin	251
Felon		arsenic sulphide	110
		calcium sulphide	218
		lobelin	479
		rhus tox	577
		veratrine	650
Fermentation		benzoic acid	147
		calcidin	217
		copper arsenite	328
		creosote	334
		emetine	375
		helenin	413
		iodoform	453
		manganese	488
		menthol	490
		mercury salicylate	491
		quinine salicylate	559
		resorcin	575
		salicylic acid	585
		zinc sulphocarbolate	674
Fever		acetanilid	27
		aconitine	28
		anemonin	59
		arsenic	98
		asclepidin	112
		atropine	136
		chionanthin	271
		delphinine	346
		digitalin	360
		leptandrin	477
		lobelin	479
		mercury	492
		nuclein	514
		quinine	564
		resorcin	575
		salicylic acid	582
		strychnine	628
		veratrine	650
		zinc sulphocarbolate	674
	bilious	bryonin	180
	debility of	cantharidin	248
	dyspnea of	aspidospermine	119
	eruptive	aconitine	42
		atropine	136
		pilocarpine	531
		veratrine	651
	feeble reaction	capsicin	254
	foul stomach	emetine	375
	from chilling	capsicin	254
	insomnia	hyoscine	426
		narceine	506
	irritative	aconitine	28
	jugulating	pilocarpine	531
	low	baptisin	140
		caffeine	198
		cypripedin	340
		zinc phosphide	671

Disease	*Phase*	*Remedy*	*Page*
Fever	malarial	cinchonidine	284
		cinchonine	285
		cornin	331
		iridin	456
		mercury	492
		picric acid	528
		quinine	563
		quinine arsenate	559
	microbic	calcium sulphide	218
	nocturnal delirium	zinc valerate	676
		menthol	491
	puerperal	aconitine	28
		benzoic acid	147
		ergotin	389
		gelseminine	398
		sodium benzoate	151
		veratrine	651
	restlessness of	camphor monobromide	232
		convallamarin	326
	septic	benzoic acid	147
		echinacea	370
	skin irritation	caffeine	198
	sores	baptisin	140
	specific	aconitine	39
	sthenic	aconitine	28
		gelseminine	398
		veratrine	651
	surgical	aconitine	28
	traumatic	aconitine	40
	typhoid	aconitine	43
	urethral	aconitine	28
	wasting	caffeine	198
		lecithin	468
Fibroids		calcidin	217
		ergotin	389
Fidgets		aconitine	28
		anemonin	59
Fissures		benzoic acid	147
		iodoform	453
		phytolaccin	526
Fistula		phytolaccin	526
Flatulence		aletrin	54
		aloin	55
		ammonium salicylate	587
		asclepidin	112
		berberine	152
		cannabis indica	240
		capsicin	255
		hydrastine	417
		menthol	492
		physostigmine	523
		picrotoxin	529
		xanthoxylin	662
Foreboding:	morbid	cicutine	275
Fractures:	ununited	lecithin	468
		zinc phosphide	671
Freckles		benzoic acid	149
Furuncles (see boils)			

G

Galactagog		papayotin	518
		pilocarpine	531

Disease	*Phase*	*Remedy*	*Page*
Galactorrhea		ergotin	389
Gallstones (see colic: hepatic)			
Ganglionic engorgements		cicutine	275
	excess	cicutine	275
Gangrene		baptisin	140
		salicylic acid	584
	pulmonary	benzoic acid	148
		echinacea	370
	senile	arsenic iodide	109
Gas poisoning—illuminating		glonoin	404
Gastralgia		acetanilid	27
		aconitine	28
		arsenic	85
		atropine	136
		benzoic acid	147
		cannabis indica	239
		cerium oxalate	261
		chelidonin	262
		cocaine	294
		codeine	299
		glonoin	404
		iridin	455
		narceine	506
		picrotoxin	531
Gastric affections		aconitine	28
		emetine	375
	atony	berberine	153
		brucine	179
		hydrastine	419
		leptandrin	477
		papayotin	518
		quassin	556
	cancer	chelidonin	262
		cicutine	275
		condurangin	318
	catarrh	geranin	403
		hydrastine	417
		juglandin	463
		myricin	504
		rhein	576
		xanthoxylin	662
		zinc oxide	668
	dilatation	berberine	152
		strychnine	628
		zinc oxide	668
	indigestion	asclepidin	112
		copper arsenite	327
		papayotin	518
		pepsin	520
	irritability	cerium oxalate	260
		cocaine	294
		collinsonin	313
		iridin	455
		pepsin	520
		zinc cyanide	667
	maladies	aconitine	28
		anemonin	59
		emetine	375
		rhus tox	577
	pain	cannabis indica	237
		cerium oxalate	260
		echinacea	370

Disease	*Phase*	*Remedy*	*Page*
Gastric affections		solanine	608
	ulcer	condurangin	318
		hydrastine	417
		rumicin	581
		zinc oxide	668
Gastrodynia		cerium oxalate	260
		gelseminine	397
		menthol	491
		nickel bromide	509
		zinc oxide	668
Gastromalaria		cornin	331
Gelsemine			397
Gelseminine			397
Genitourinary affections		arbutin	77
		barosmin	145
	atony	chimaphilin	269
	inflammation	camphor monobromide	232
	debility	cantharidin	248
		helonin	416
		rhus tox	577
Geranin			403
Glands enlarged (see adenitis)		apiol	65
		arsenic iodide	109
		calcidin	213
		echinacea	370
		iodoform	453
		juglandin	463
		mercury biniodide	491
		phytolaccin	526
	scrofulous	cicutine	275
Glaucoma		arecoline	83
		physostigmine	523
		pilocarpine	541
Gleet		arbutin	77
		benzoic acid	147
		cantharidin	248
		collinsonin	313
		copper arsenite	330
		cubebin	337
		iodoform	453
		piperine	547
		senecin	602
Glonoin			404
	habit		404
Glottis:	edema	atropine	136
Glycosuria (see diabetes)		ergotin	382
Goiter		ammonium chloride	58
		berberine	152
		calcidin	216
		chromium sulphate	273
		iodoform	453
		iridin	455
		stillingin	625
	exophthalmic (see exophthalmos)		
	with irritability	nickel bromide	510
Gold			408
Gonorrhea		aconitine	28
		alnuin	54
		apiol	65
		arbutin	77
		arsenic sulphide	111
		barosmin	145

Disease	*Phase*	*Remedy*	*Page*
Gonorrhea		benzoic acid	147
		boldine	174
		calcium sulphide	227
		camphor monobromide	232
		cannabis indica	240
		chimaphilin	269
		cocaine	295
		colchicine	312
		cubebin	337
		gelseminine	400
		hydrastine	418
		iodoform	453
		iridin	456
		iron	460
		macrotin	484
		pilocarpine	531
		resorcin	575
		senecin	602
		sodium benzoate	151
	acute	gelseminine	400
		veratrine	651
	chronic	cantharidin	244
	orchitis	anemonin	59
	painful	menthol	490
Gossypin			410
Gout		aconitine	28
		arbutin	77
		asparagin	114
		atropine	136
		benzoic acid	149
		calcalith	211
		cannabis indica	239
		chimaphilin	269
		colchicine	311
		lithium benzoate	150
		salicylic acid	582
	tophi	ammonium benzoate	150
Gravel		ammonium benzoate	150
		calcalith	211
		chimaphilin	269
		collinsonin	313
		eupurpurin	396
	pain	cannabis indica	237
	uric	lithium benzoate	150
Gregory's salt			410
Growth retarded		lecithin	468
Guaranine			411

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Hair (see alopecia)			
Hallucinations		hyoscine	426
Hamamelin			411
Hay fever		alnuin	54
		arsenic	85
		aspidospermine	115
		atropine	136
		calcalith	208
		calcidin	213
		cannabis indica	240
		cocaine	285

Disease	*Phase*	*Remedy*	*Page*
Headache		acetanilid	27
		æsculin	49
		atropine	136
		boldine	173
		caffeine valerate	193
		chelidonin	264
		duboisine	370
		gelseminine	400
		guaranine	411
		leptandrin	477
		menthol	491
		narceine	506
		zinc valerate	676
	anemic	hyoscyamine	447
		glonoin	404
		iron bromide	461
	autotoxemic	aloin	55
		caffeine	199
	constant	cannabis indica	239
	dull frontal	bryonin	182
		caulophyllin	262
		eupurpurin	396
		hyoscyamine	446
		leptandrin	477, 479
		podophyllin	549
	from acidity	caffeine	199
	from blasting powder	iodoform	453
	indigestion	asclepidin	112
	menopause	cactin	184
	menstrual	anemonin	59
		avenine	138
		gelseminine	400
		veratrine	651
	nervous	anemonin	59
	butyl-chloral-hydrate		182
		camphor monobromide	232
		cypripedin	340
		menthol	491
	occipital	avenine	138
		zinc phosphide	671
	ocular	atropine	136
		butyl-chloral-hydrate	182
		gelseminine	400
	periodic	bebeerine	146
	pregnancy	anemonin	59
	rheumatic	bryonin	179
		macrotin	484
	sick	butyl-chloral-hydrate	182
		calcalith	208
		cascarin	257
		iridin	455
		podophyllin	549
		sanguinarine	588
	uric	colchicine	312
Heart	aortic disease	cactin	188
		strophanthin	627
	arrhythmia	convallamarin	326
		zinc cyanide	667
	bicycle	collinsonin	313
	clot	brucine	176
	digitalin for		359
	dilatation	apocynin	68

Disease	*Phase*	*Remedy*	*Page*
Heart		iron	460
	dilatation not fatty	berberine	152
	disease	acetanilid	27
		adonidin	47
		antimony arsenate	64
		apocynin	68
		atropine	136
		cannabis indica	237
		convallamarin	324
		lycopin	482
	cough	collinsonin	313
	functional	cactin	187
		caffeine	198, 201
	nervous	scutellarin	601
	old age	sparteine	617
		strophanthin	626
	failure	atropine	136
		brucine	177
		caffeine	207
		camphor monobromide	232
		glonoin	404
	from strain	brucine	176
	fatty	caffeine	201, 207
		iron	460
	fluttering	aconitine	28
		digitalin	348
	hypertrophy	aconitine	28
		barium chloride	144
		calcidin	216
		gelseminine	400
	irregular	veratrine	651
		aconitine	28
		aspidospermine	115
		cactin	184
		copper arsenite	327
		gelseminine	400
		lycopin	482
	mitral disease	convallamarin	326
		digitalin	349
		lecithin	470
		sparteine	621
	rheumatic and gouty	bryonin	179
		collinsonin	313
		veratrine	651
	strain	bryonin	179
	tobacco	aconitine	28
		apocynin	68
		sparteine	621
	weak	avenine	138
		barium chloride	144
		cactin	184
		caffeine	201
		cocaine	285
		digitalin	349
		macrotin	484
		sparteine	621
		strophanthin	626
		strychnine	628
		zinc phosphide	671
Heartburn		arsenic	85
Heat exhaustion		berberine	152
		brucine	176

Disease	*Phase*	*Remedy*	*Page*
Heat Exhaustion		caffeine	201
		glonoin	406
		hyoscyamine	446
Heat flashes at menopause		glonoin	406
Hectic sweats		agaricin	50
Helenin			413
Helonin			416
Hematemesis		atropine	136
		condurangin	320
		emetine	380
		ergotin	382
Hematuria		alnuin	54
		arbutin	77
		cannabis indica	240
		cantharidin	247
		chimaphilin	269
		ergotin	382
		eupurpurin	396
		geranin	403
		senecin	602
Hemianopsia		cannabis indica	240
Hemicrania		arsenic	85
		benzoic acid	147
		bryonin	179
		caffeine	201, 207
		quinine	559
Hemiplegia		avenine	138
Hemoglobinuria		caffeine	200
Hemophilia		atropine	136
		cocaine	296
		ergotin	382
		stypticin	509
Hemoptysis		atropine	136
		cetrarin	262
		digitalin	367
		emetine	378
		ergotin	382
		eupurpurin	396
		gelseminine	400
		gossypin	410
		hydrastinine	424
		iodoform	453
		lycopin	482
		narcotine	508
		stypticin	507
Hemorrhage		acetanilid	27
		alnuin	54
		atropine	122, 132
		digitalin	362
		emetine	378
		ergotin	386
		geranin	403
		gossypin	410
		hydrastine	417
		hydrastinine	424
		quinine	559
	acute	veratrine	651
	anemic	iron	459
	capillary	cocaine	296
		senecin	602
	climacteric	hydrastinine	424
		stypticin	508

Disease	*Phase*	*Remedy*	*Page*
Hemorrhage	from cavities	stypticin	509
	intestinal	atropine	136
	oozing	hamamelin	412
	passive	apocynin	68
		collinsonin	313
		hamamelin	412
		iron	459
	postpartum	atropine	136
		capsicin	255
		caulophyllin	257
		emetine	379
		ergotin	386
		glonoin	406
		iron	459
		strychnine	628
	rectal	atropine	136
	retinal	benzoic acid	147
		ergotin	386
	tooth cavity	hamamelin	412
		stypticin	508
	uterine	atropine	136
		capsicin	255
		ergotin	386
		gossypin	410
		hydrastinine	424
Hemorrhoids		æsculin	49
		aloin	55
		arsenic	85
		atropine	136
		capsicin	253
		cascarin	257
		chelidonin	264
		cocaine	285
		collinsonin	313
		echinacea	373
		ergotin	386
		hamamelin	411
		iodoform	453
		jalapin	463
		juglandin	463
		phytolaccin	526
		piperine	546
		podophyllin	547
		rhein	576
		stillingin	625
		strychnine	633
	passive	berberine	152
		cantharidin	249
		capsicin	253
	pregnancy	collinsonin	313
Hepatic maladies		chionanthin	270
		helonin	416
		jalapin	463
	alcoholic	boldine	173
	chronic	boldine	173
	congestive	boldine	173
		hydrastine	411
	insufficiency	bilein	155
	obstruction	colchicine	312
	malarial	boldine	173
	pain	hyoscyamine	447

Disease	*Phase*	*Remedy*	*Page*
Hepatic maladies		leptandrin	477
	tropical	boldine	173
Hepatitis		aconitine	28
		cicutine	275
		iridin	455
		phytolaccin	526
		veratrine	651
Hernia:	strangulated	atropine	122, 130
		caffeine	201
		hyoscyamine	447
		lobelin	479
		strychnine	633
Herpes		alnuin	54
		arsenic	96
	zoster	aconitine	28
		atropine	136
		zinc phosphide	671
Hiccough		atropine	120
		caffeine	202, 206
		caulophyllin	259
		cicutine	280
		cocaine	295
		dioscorein	367
		hyoscine	428
		hyoscyamine	447
		pilocarpine	531
Hoarseness		calcidin	213
		cantharidin	249
		capsicin	253
		potassium bichromate	550
Hodgkin's disease		arsenic	85
Homatropine			120
Horse flies		baptisin	139
Hunger		caffeine	201
Hydrastine			417
Hydrastinine			421
Hydrocephalus		apocynin	48
		elaterin	374
		pilocarpine	531
Hydropericardium		caffeine	198
Hydrophobia		camphor monobromide	235
		cicutine	279
		curarine	340
		echinacea	370
		pilocarpine	541
Hyoscine			426
Hyoscyamine			446
Hyoscyamus			446
Hyperemia		aconitine	28
		camphor monobromide	232
	cerebral	digitalin	362
		hyoscine	427
		veratrine	651
	hepatic	elaterin	374
		phytolaccin	526
	pulmonary	aconitine	28
		asclepidin	112
		veratrine	651
	renal	atropine	136
	visceral	aconitine	28
Hyperesthesia:	infantile	aconitine	45
		cicutine	275

Disease	*Phase*	*Remedy*	*Page*
Hyperesthesia:	sexual	salicin	582
Hyperidrosis		agaricin	50
		pilocarpine	531
Hyperpyrexia		acetanilid	28
		aspidospermine	115
		veratrine	651
Hyperlactation		agaricin	50
		apiol	65
Hypersecretion		atropine	136
Hypochondria		aloin	55
		arsenic	103
		atropine	120
		bryonin	182
		caffeine	201
		camphor monobromide	232
		colchicine	312
		cypripedin	340
		gold	408
		macrotin	484
		strychnine	636
		zinc cyanide	667
	from renal insufficiency	colchicine	302
	of menopause	cannabis indica	240
Hypogastric plexus irritation		caulophyllin	258
Hypoleucocytosis		lecithin	468
		nuclein	511
Hyposecretion		emetine	375
		lobelin	478
Hysteria		aloin	55
		anemonin	59
		apomorphine	71
		atropine	136
		bebeerine	146
		camphor monobromide	232
		cannabis indica	240
		caulophyllin	258
		chromium sulphate	274
		cicutine	275
		cocaine	295
		cypripedin	340
		delphinine	347
		gelseminine	400
		hyoscine	427
		lobelin	478
		macrotin	484
		narceine	505
		nickel bromide	509
		pilocarpine	531
		scutellarin	601
		strychnine	636
		viburnin	660
		zinc cyanide	667
		zinc oxide	668
	headache	cactin	184
		caffeine	201
Hystero-epilepsy		camphor monobromide	232
		cocaine	295
		pilocarpine	531

I

Ichthyosis		arsenic sulphide	111
Ileocolitis		emetine	378

Disease	*Phase*	*Remedy*	*Page*
Impaction of feces		atropine	130
		hyoscyamine	448
Impetigo		alnuin	54
		juglandin	463
Impotence		asparagin	114
		atropine	120
		cactin	184
		cannabis indica	240
		cantharidin	248
		capsicin	251
		cornin	331
		eupurpurin	396
		gold	408
		gossypin	410
		lecithin	468
		senecin	603
		strychnine	628
		yohimbine	664
		zinc phosphide	671
Incontinence (see enuresis)			
Indigestion		alnuin	54
		arsenic	85
		bryonin	179
		diastase	348
		emetine	380
		euonymin	394
		iron	460
		juglandin	463
		lobelin	479
		menthol	491
		mercury	494
		papayotin	517
		pepsin	520
	atonic	bebeerine	146
		berberine	152
		hydrastine	417
		quassin	552
	of albumin	pepsin	520
	of anything	papayotin	517
	of starch	diastase	348
Infections		calcium sulphide	218
		nuclein	515
Inflammation	acute	aconitine	38, 42
		gelseminine	400
		mercury	494
		narceine	506
		nuclein	511
		quinine	564
		veratrine	651
	chronic	bryonin	180
	mammary	phytolaccin	526
Influenza		acetanilid	27
		anemonin	59
		arsenic	97
		asclepidin	112
		atropine	136
		brucine	176
		bryonin	180
		calcidin	216
		camphor monobromide	232
		gelseminine	400
		nuclein	515

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Influenza		pilocarpine	531
	sweating	picrotoxin	529
		salicylic acid	586
Insanity	delirium	aconitine	41, 43
		apomorphine	71
		colocynthin	315
		gelseminine	397
		hyoscyamine	449
		veratrine	651
	fear of	cicutine	275
Insect bites		emetine	397
Insomnia		aconitine	40
		antimony arsenate	64
		atropine	136
		boldine	173
		caulophyllin	259
		codeine	300
		convallamarin	326
		cypripedin	340
		digitalin	366
		hyoscine	427
		morphine	499
		zinc phosphide	671
		zinc valerate	676
	fatigue	camphor monobromide	233
	from cough	narceine	506
	from pain	butyl-chloral-hydrate	182
		morphine	499
	of melancholy	codeine	300
		hyoscyamine	448
	nervous exhaustion	camphor monobromide	233
	restlessness	leptandrin	477
		scutellarin	602
Intestinal antiseptics		benzoates	150
		calcidin	213
		copper arsenite	327
		creosote	334
		iodoform	453
		mercury biniodide	491
		potassium permanganate	551
		quinine	559
		quinine salicylate	559
		resorcin	575
		salicylic acid	582
		zinc sulphocarbolate	674
	atony	berberine	152
		corydalin	332
		leptandrin	477
	obstruction	atropine	131
		hyoscyamine	448
		lobelin	479
	relaxation	codeine	300
Invagination		atropine	136
Iodine			213
Iodoform			451
Iridin			455
Iritis		aconitine	28
		atropine	137
		bryonin	179
		cocaine	296
		echinacea	370
		iridin	456

Disease	*Phase*	*Remedy*	*Page*
Iritis		mercury biniodide	491
		pilocarpine	531
		salicylic acid	582
	rheumatic	aconitine	49
Iron			457
	arsenate		461
	iodide		461
	phosphate		462
	valerate		462
Itching		chelidonin	264
		pilocarpine	531
	anal	æsculin	49
	local	benzoic acid	147

J

Jalapin			462
Jaundice		apocynin	68
		boldine	173
		bryonin	179
		caffeine	201
		cascarin	257
		chelidonin	264
		chionanthin	270
		euonymin	395
		iodoform	453
		leptandrin	477
		pilocarpine	541
		podophyllin	547
	catarrhal	emetine	375
		sanguinarine	588
	chronic	iridin	456
		juglandin	463
	malarial	arsenic	85
		caffeine	193
		iridin	455
	malignant	zinc phosphide	671
	pregnancy or childhood	chionanthin	270
	spasmodic	caffeine	193
Jervine			649
Joint diseases		calcium sulphide	220
		iodoform	453
		lecithin	470
Juglandin			463

K

Keratitis		atropine	136
Kidneys	congestion	capsicin	251
	test of permeability (see nephritis)	asparagin	113
Koussein			467

L

Labor ailments		atropine	136
		hyoscine	426
	chills following	strychnine	628
	false pains	caulophyllin	257
	rigid os	apomorphine	71
		lobelin	478
	weak pains	caulophyllin	257
		eupurpurin	396
		morphine	495

Disease	*Phase*	*Remedy*	*Page*
Lactorrhea		atropine	120
Laloneurosis		duboisine	369
Languish on rising		avenine	139
Larynx	irritation	menthol	491
	inflammation	calcium sulphide	218
	spasm	cicutine	275
Laryngismus stridulus		atropine	137
		cocaine	296
		emetine	375
		gelseminine	397
		glonoin	404
		hyoscyamine	447
		lobelin	478
Laryngitis		aconitine	28
		benzoic acid	148
		camphor monobromide	240
		cantharidin	248
		cicutine	280
		collinsonin	313
		emetine	378
		iodoform	454
		lobelin	479
		pilocarpine	531
		zinc cyanide	667
	acute	apomorphine	71
Larynx	cancer	chelidonin	262
	diphtheria	baptisin	139
	tubercle	papayotin	517
Laudanine			495
Laxation	passive	berberine	152
Lead (see colic)			
Lecithin			468
Leptandrin			477
Leprosy		nuclein	515
		thiosinamine	638
Leucocythemia		arsenic	85
		iridin	455
		manganese	488
		nuclein	511
Leucoma:	corneal	anemonin	59
Leucorrhea		alnuin	54
		anemonin	59
		apocynin	68
		arbutin	77
		baptisin	139
		bebeerine	146
		calcium sulphide	229
		cantharidin	248
		caulophyllin	258
		collinsonin	313
		corydalin	332
		eupurpurin	396
		hamamelin	411
		hydrastine	417
		iridin	455
		iron	457
		phytolaccin	526
		resorcin	575
		salicin	582
		senecin	602
Leukemia		arsenic	96
		berberine	153

Disease	*Phase*	*Remedy*	*Page*
Leukemia		picric acid	528
	splenic	arsenic	96
Lichen		arsenic	96
		cantharidin	248
		iron arsenate	461
		juglandin	463
	ruber	arsenic	96
Lientery		copper arsenite	327
		quassin	557
Lithemia		arbutin	77
		caffeine	193
	(see uric acid)		
Lithium benzoate			150
Liver	aching	æsculin	49
	affections	baptisin	139
		boldine	173
		chionanthin	270
		dioscorein	367
		iridin	455
		nuclein	511
	atony	leptandrin	477
	cancer pains	dioscorein	367
	cirrhosis	convallamarin	326
		gold	408
		iodoform	453
		stillingin	625
	enlargement	euonymin	394
		phytolaccin	526
		podophyllin	547
	fatty	zinc phosphide	671
	hypertrophy	boldine	173
	obstructive catarrh	hydrastine	417
	torpid	ammonium chloride	58
		bryonin	179
		collinsonin	313
		euonymin	394
		iridin	457
		juglandin	463
		leptandrin	477
		mercury	492
		podophyllin	547
		sodium benzoate	151
	with heart disease	berberine	152
Lobelin			478
Lumbago		acetanilid	27
		atropine	137
		camphor monobromide	232
		euonymin	394
		gelseminine	400
		juglandin	463
		macrotin	484
		rhus tox	580
		salicylic acid	582
Lumbricoid worms		santonin	590
Lung diseases		aconitine	28
		antimony arsenate	64
		lobelin	478
		pilocarpine	547
	congestion	jalapin	462
	edema	benzoic acid	147
		caffeine	200
	gangrene	ammonium salicylate	582

Disease	*Phase*	*Remedy*	*Page*
Lung diseases	hyperemia	lycopin	482
Lupus		arsenic	107
		cantharidin	247
		gold	409
		iron arsenate	461
		quinine	565
		sanguinarine	588
		zinc phosphide	671
Lycopin			482
Lymphatic engorgement		alnuin	54
		apocynin	68
		arsenic	96
Lymphoma.	malignant	corydalin	332
		gold	409
		phytolaccin	526
		arsenic	96, 99

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Macrotin			484
Malaise		leptandrin	477
Malaria		aconitine	28
		æsculin	49
		agaricin	50
		ammonium chloride	58
		apiol	65
		apocynin	68
		apomorphine	71
		arbutin	77
		arsenic	96, 98
		bebeerine	146
		berberine	153
		calcium sulphide	227
		cinchonidine	284
		cinchonine	285
		cornin	331
		dioscorein	367
		mercury	494
		narcotine	507
		picric acid	528
		piperine	546
		quinine	569
		salicin	582
		strophanthin	626
	algid	capsicin	253
		glonoin	406
		hyoscyamine	446
	cachexia	corydalin	332
		iron	459
	chills	atropine	137
		capsicin	253
		glonoin	406
		morphine	495
		pilocarpine	531
	dyspepsia	chionanthin	270
		echinacea	370
		emetine	375
		leptandrin	477
		sodium benzoate	151
		sulphocarbolates	674
	hematuria	strychnine	628
Malignancy		echinacea	370

Disease	*Phase*	*Remedy*	*Page*
Malnutrition		lecithin	468
Mandragora			120
Mandragorine			120
Manganese			487
Mania		atropine	137
		baptisin	141
		cannabis indica	239, 244
		cicutine	282
		digitalin	362
		hyoscyamine	447
		pilocarpine	531
		veratrine	651
	acute	scopolamine	600
		veratrine	651
	excitement	camphor monobromide	230
		gelseminine	400
		hyoscine	430
	hysteric	apomorphine	71
	of low fevers	camphor monobromide	230
Marasmus		alnuin	54
		lecithin	468
		nuclein	511
Mastitis		aconitine	28
		alnuin	54
		apiol	65
		atropine	137
		chimaphilin	269
		phytolaccin	527
	acute	bryonin	179
	milk stopped	pilocarpine	531
Masturbation		avenine	138
		cactin	184
		calcium sulphide	218
		cantharidin	248
Measles		aconitine	28
		anemonin	59
		atropine	137
		baptisin	142
		calcium sulphide	226
		echinacea	370
		emetine	381
		pilocarpine	531
		quinine	565
		rhus tox	577
Melancholy		aloin	55
		arsenic	85
		atropine	137
		baptisin	141
		caffeine	193
		camphor monobromide	232
		cannabis indica	240
		cocaine	295
		codeine	299
		colchicine	312
		cypripedin	340
		macrotin	484
		nickel bromide	509
Membrane: false		camphor monobromide	232
Meniere's disease		gelseminine	400
		quinine	565
		salicylic acid	582
Meningitis		aconitine	28

Disease	*Phase*	*Remedy*	*Page*
Meningitis		elaterin	374
		ergotin	382
		gelseminine	400
		hyoscine	427
		hyoscyamine	449
		iodoform	453
		veratrine	651
	headache	bryonin	179
	tubercular	cicutine	280
Menispermin			490
Menopause:	nervousness	cicutine	275
	anemia	iron	457
	headache	cannabis indica	239
	and flushes	gelseminine	400
	hemorrhages	cannabis indica	240
	unrest, etc.	macrotin	484
Menorrhagia		aconitine	28
		apocynin	68
		arbutin	77
		atropine	137
		bebeerine	146
		berberine	153
		cannabis indica	240
		cantharidin	248
		emetine	380
		ergotin	382
		gossypin	410
		hydrastinine	424
		senecin	602
	passive	apocynin	68
	young girls	apocynin	68
		hydrastinine	424
		stypticin	508
Menstrual disorders		arsenic	97
		berberine	152
		bryonin	179
		caulophyllin	258
		collinsonin	313
		corydalin	332
		dioscorein	367
		eupurpurin	396
		gelseminine	400
		gold	408
		helonin	416
		hydrastine	417
		macrotin	484
		viburnin	661
	fetor	apiol	65
Mental depression		leptandrin	477
	aberration	cicutine	275
	failure	gold	408
		lecithin	468
		nuclein	511
	torpor from sex excess	cypripedin	340
		zinc phosphide	671
Menthol			490
Mercury			491
	pharyngitis	baptisin	139
	salivation	atropine	137
		calcidin	213
		hydrastine	417
Metabolism:	poor	chimaphilin	269

Disease	*Phase*	*Remedy*	*Page*
Metabolism:	poor	corydalin	332
		nuclein	511
Metritis		aconitine	28
		caulophyllin	258
		cubebin	337
	acute	pilocarpine	531
	chronic	berberine	152
		cannabis indica	240
		hydrastine	417
Metrorrhagia		apocynin	68
		cannabis indica	240
		emetine	375
		gossypin	410
		hydrastinine	424
		senecin	602
		viburnin	661
Microbic infection: to inhibit		calcium sulphide	218
Micturition: frequent		arbutin	77
		barosmin	145
Migraine		butyl-chloral-hydrate	182
		caffeine	193
		cannabis indica	239
		cocaine	295
		chromium sulphate	274
		gelseminine	400
		picrotoxin	529
		salicylic acid	582
Milk: scanty		pilocarpine	531
	sickness	atropine	137
Morphine			495
	habit	avenine	139
		cannabis indica	244
		capsicin	251
		cocaine	293
		cypripedin	340
		gelseminine	397
		hyoscine	427
		nuclein	511
		physostigmine	523
		sparteine	621
		zinc valerate	676
	treatment		499
	poisoning	glonoin	404
		potassium permanganate	551
Mosquitoes		calcium sulphide	218
Moth patches		benzoic acid	147
		caulophyllin	257
Motor irritability		cicutine	275
		curarine	338
Mucous atony		berberine	152
		hydrastine	417
	fluxes	atropine	137
		codeine	300
		hamamelin	411
		hydrastine	417
		strychnine	628
		xanthoxylin	662
	insensibility	sanguinarine	588
		scillitin	591
	reflex irritability	atropine	120
		hydrastine	417
Mumps		calcium sulphide	218

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Mumps		pilocarpine	531
Murrain in horses		juglandin	463
Mushroom poisoning		strychnine	633
Muscular:	soreness	hamamelin	411
	aching	macrotin	484
	spasm	gelseminine	397
	tremor	duboisine	369
	weakness	caffeine	193
		veratrine	651
Myalgia		aconitine	28
		ammonium chloride	58
		atropine	137
		calcalith	208
		camphor monobromide	230
		colchicine	312
		gelseminine	397
		hydrastine	417
		macrotin	484
		rhus tox	580
		salicylic acid	585
Myelitis		atropine	137
		ergotin	382
		pilocarpine	531
Myocarditis		arsenic	96
		caffeine	199
		sparteine	620
Myoma		berberine	152
		hydrastinine	425

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Narceine			504
Narcomania		cannabis indica	240
Narcotics: abuse of		caffeine	204
Narcotine			507
Nausea		cerium oxalate	260
		copper arsenite	330
		creosote	334
		picrotoxin	529
		menthol	491
Necrosis		zinc phosphide	671
Neoplasms: malignant		chelidonin	262
Nephritis		aconitine	28
		adonidin	47
		arbutin	77
		arsenic	97
		atropine	137
		benzoic acid	148
		caffeine	198
		calcium benzoate	150
		cannabis indica	240
		cantharidin	247
		cerium oxalate	260
		chimaphilin	269
		convallamarin	326
		creosote	334
		euonymin	394
		gelseminine	400
		helonin	416
		hydrastine	417
		hydrastinine	425
	acute	aconitine	28

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Nephritis	acute	apocynin	68
		cantharidin	247
		gelseminine	400
	alcoholic	cantharidin	247
	chronic	colocynthin	318
	cirrhotic	glonoin	405
		veratrine	651
	desquamative	apocynin	68
		arbutin	77
		capsicin	251
		hydrastine	417
		iron	459
	dyspnea of (see uremia)	strophanthin	627
Nephrolithiasis		calcalith	208
Nervous affections		camphor monobromide	232
		lecithin	468
	excitement	cactin	184
		nickel bromide	510
	headache	caffeine	193
		cocaine	285
		zinc valerate	676
	irritability	aspidospermine	115
		camphor monobromide	232
		cocaine	285
		cypripedin	340
		dioscorein	367
		gelseminine	400
		lobelin	470
		physostigmine	521
	merycismus	eupurpurin	396
		zinc cyanide	667
	tremors	avenine	138
	vomiting	zinc cyanide	667
	wakefulness	nickel bromide	510
Nervousness		aconitine	28
		anemonin	59
		arsenic	85
		camphor monobromide	230
		scutellarin	601
		zinc valerate	676
Neuralgia		acetanilid	27
		aconitine	40
		apiol	63
		arsenic	98
		asclepidin	112
		atropine	137
		bryonin	179
		caffeine	199, 207
		camphor monobromide	232
		cannabis indica	239
		chelidonin	264
		cicutine	279
		cocaine	293
		codeine	300
		convallamarin	326
		delphinine	346
		gelseminine	397
		hyoscyamine	447
		iodoform	452
		iron	459
		menthol	491

Disease	*Phase*	*Remedy*	*Page*
Neuralgia		morphine	499
		narceine	506
		quinine	570
		salicin	582
		solanine	608
		strychnine	634
		veratrine	651
		zinc phosphide	671
	cardiac (see angina)		
	chlorotic	cicutine	275
	congestive	gelseminine	397
	diathetic	aconitine	40
	facial	butyl-chloral-hydrate	182
	from carious teeth	butyl-chloral-hydrate	182
	intercostal	aconitine	28
		asclepidin	112
		zinc phosphide	671
	lithemic	caffeine	201
		euonymin	394
	ocular	physostigmine	523
	strain	hyoscyamine	447
	of exhaustion	atropine	137
	ovarian	atropine	137
		gelseminine	400
		macrotin	485
	periodic	bebeerine	146
		cinchonidine salicylate	284
	rectal	æsculin	49
	reflex	arsenic	85
	trigeminal	atropine	137
		butyl-chloral-hydrate	182
	visceral	æsculin	49
	with twitching	gelseminine	400
	weak heart	bryonin	179
Neuralgic pains		cicutine	275
Neurasthenia		anemonin	59
		arsenic	85
		avenine	138
		cactin	184
		chromium sulphate	272
		codeine	300
		gold	408
		lecithin	470
		nuclein	511
		quinine	559
		strychnine	636
		yohimbine	664
		zinc phosphide	671
Neuritis: optic		pilocarpine	531
Neuropathies: central		acetanilid	27
		aconitine	28
Neuroses		antimony arsenate	64
		atropine	131
	functional	arsenic	97, 98
	intermittent	caffeine arsenate	193
	local	zinc phosphide	392
	paroxysmal	quinine arsenate	559
Nickel bromide			509
Nicotism		caffeine	193
Night-sweats		agaricin	50
		apiol	65
		atropine	137

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Night-sweats		calcidin	216
		hydrastine	419
		picrotoxin	530
		pilocarpine	531
		quinine	559
		zinc oxide	668
	hectic	eupurpurin	396
		geranin	403
		helenin	413
	phthisical	calcium sulphocarbolate	674
		hydrastinine	425
		physostigmine	523
		pilocarpine	531
	terrors	hyoscine	427
		hyoscyamine	446
Nipples: fissured		baptisin	139
		benzoic acid	147
		hydrastine	419
Nuclein			511
Nursing sore mouth		juglandin	463
		rumicin	581
Nymphomania		calcium sulphide	218
		camphor monobromide	232
		gold bromide	408
		salicin	582
		zinc valerate	676

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Obesity		atropine	137
		berberine	152
		caffeine	207
		calcidin	217
		phytolaccin	527
Odontalgia		atropine	120
Oesophagismus		atropine	137
Old age: maladies of		arbutin	77
		arsenic iodide	109
		emetine	375
		lecithin	470
		nuclein	511
		sanguinarine	588
		sparteine	617
		yohimbine	664
		zinc phosphide	671
Oliguria		colchicine	312
		convallamarin	324
		digitalin	349
Opacities: corneal		pilocarpine	531
		thiosinamine	638
Ophthalmia		anemonin	59
		baptisin	139
		capsicin	255
	strumous	bebeerine	146
		cicutine	275
Opiate nausea		cerium oxalate	260
Opiate poisoning		glonoin	407
		morphine	503
		strychnine	628
Optic nerve atrophy		anemonin	59
Orchialgia		caulophyllin	259

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Orchitis		aconitine	28
		atropine	137
		macrotin	485
		veratrine	651
	chronic	bryonin	180
	mumps	phytolaccin	526
Osteomalacia		zinc phosphide	671
Otalgia (see earache)		atropine	137
Otitis		aconitine	42
		atropine	137
		delphinine	347
	media	sanguinarine	588
Ovaralgia		colocynthin	318
Ovaritis		iodoform	453
		pilocarpine	531
		salicin	582
Ovary:	pain	cicutine	275
		dioscorein	367
		hyoscyamine	447
Overwork:	mental	lecithin	468
		nuclein	511
		zinc phosphide	671
Ozena		cantharidin	244
		papayotin	518
		phytolaccin	526
		sanguinarine	588

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Pain:	spasmodic	atropine	131
		hyoscyamine	447
	alimentary canal	codeine	300
	bones	iodoform	453
	burning	rhus tox	577
	cancer	cicutine	275
	chest	lobelin	478
	false labor	caulophyllin	258
	gastrointestinal	chelidonin	262
	habit	strychnine	628
	hyperesthetic	cicutine	275
	inflammatory	narceine	506
	wounds	morphine	499
	in joints after scarlatina	cypripedin	340
	intense	hyoscine	445
		zinc cyanide	667
	muscular	hydrastine	417
		macrotin	484
		potassium bichromate	550
	nervous	cypripedin	340
	pelvic	colocynthin	318
		salicylic acid	582
	senile gangrene	arsenic iodide	109
	toes or fingers	caulophyllin	258
Palpitation		avenine	138
		caffeine	201
		camphor monobromide	232
		chelidonin	262
		convallamarin	324
		digitalin	349
		gelseminine	400
		glonoin	404
		sparteine	617

Disease	*Phase*	*Remedy*	*Page*
Palpitation		strophanthin	626
		veratrine	651
	flatulent	menthol	490
Papayotin			517
Paralysis		æsculin	49
		arsenic iodide	109
		atropine	137
		avenine	138
		cactin	184
		capsicin	254
		colocynthin	315
		croton oil	335
		elaterin	373
		iodoform	453
		phytolaccin	526
		mercury biniodide	491
		rhus tox	577
		scopolamine	600
		strychnine	634
		zinc phosphide	671
	agitans	avenine	138
		barium chloride	142
		camphor monobromide	232
		cannabis indica	239
		cicutine	275
		cocaine	295
		curarine	340
		duboisine	369
		hyoscyamine	447
		picrotoxin	529
		scutellarin	602
		viburnin	661
		zinc phosphide	671
	cardiac	convallamarin	324
	digestive	capsicin	254
	diphtheritic	avenine	138
		strychnine	628
	of aged	avenine	138
		strychnine	628
	of bladder	arbutin	77
		strychnine	628
	of children	brucine	176
	of insane	gold	408
		lecithin	468
		nuclein	511
		zinc phosphide	671
	to quiet tremor	hyoscine	429
Paraplegia		anemonin	59
Parasites		calcium sulphide	218
Pareses		hyoscyamine	447
Paresthesia		aconitine	28
Parotitis		chimaphilin	269
		phytolaccin	526
		rhus tox	577
Pediculi		picrotoxin	529
		quassin	552
Pellagra		arsenic	98
Pelletierine			519
Pemphigus		arsenic	98
		juglandin	463
Pepsin			520
Pericarditis		aconitine	28

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Pericarditis		arsenic	96
		asclepidin	112
		bryonin	179
		cactin	184
		caffeine	198
		colchicine	302
		convallamarin	324
		iodoform	453
		lycopin	482
		macrotin	484
		mercury biniodide	491
		veratrine	651
Peristalsis:	exaggerated	atropine	138
		codeine	277
Peritonitis		aconitine	38, 42
		asclepidin	112
		atropine	120
		bryonin	179
		iodoform	453
		morphine	495
		veratrine	651
Perityphlitis (see appendicitis)		codeine	300
		echinacea	370
		hyoscyamine	448
Perspiration:	excessive (see night sweats)	atropine	137
	in summer	berberine	152
Petit mal		camphor monobromide	230
Phagedena		baptisin	140
Pharyngitis		aconitine	28
		atropine	137
		capsicin	251
		caulophyllin	257
		hamamelin	411
		hydrastine	417
		potassium bichromate	551
	clergyman's	calcidin	216
		collinsonin	313
	follicular	nuclein	515
	singer's	calcidin	216
Phlebitis:	crural	anemonin	59
Phlegmasia dolens		hamamelin	412
Phosphaturia		benzoic acid	147
		helonin	416
Phosphorus			669
Photophobia		aconitine	28
		atropine	137
		cicutine	275
		codeine	299
		physostigmine	523
Phthisis		aconitine	42
		arsenic	85
		asclepidin	112
		atropine	131, 137
		bryonin	179
		caffeine	206
		calcium sulphide	227
		calcium sulphocarbolate	674
		cantharidin	248
		cicutine	280
		cocaine	294
		creosote	334

Disease	*Phase*	*Remedy*	*Page*
Phthisis		euonymin	394
		geranin	403
		gold	409
		helenin	414
		iodoform	452
		iron	460
		lecithin	470
		lycopin	482
		nuclein	515
		physostigmine	523
		potassium cantharidate	244
		sanguinarine	588
		sodium benzoate	151
		strychnine	635
	bad breath	salicylic acid	582
	colliquative sweats	cotoin	333
	cough	collinsonin	313
	advanced	cannabis indica	240
	dry	lobelin	478
	diarrhea	calcium sulphocarbolate	674
		cotoin	333
		salicin	582
	dyspepsia and cough	cerium oxalate	261
	dyspnea	aspidospermine	115
		calcidin	216
		convallamarin	326
	early cough	emetine	380
		helenin	414
	fever	aconitine	28
		cinchonidine salicylate	284
		digitalin	349
		quinine salicylate	570
	fibroid	emetine	380
	incipient	cetrarin	262
		lycopin	482
	incurable	cannabis indica	240
	late cough	codeine	300
	night-cough	calcidin	216
	night sweats	agaricin	50
		apiol	65
		atropine	138
		bebeerine	146
		euonymin	394
		hydrastinine	425
	sputa: fetid	sodium benzoate	151
Physostigmine			521
	poisoning		525
Phytolaccin			526
Picric acid			528
Picrotoxin			529
Pilocarpine			531
Piperine			546
Pityriasis		berberine	152
	versicolor	benzoic acid	149
Plethora		aconitine	28
		colchicine	312
	abdominal	aesculin	49
		chelidonin	263
Pleurisy		aconitine	38, 42
		arsenic iodide	96
		asclepidin	112
		atropine	137

Disease	*Phase*	*Remedy*	*Page*
Pleurisy		bryonin	180
		caffeine	198
		iodoform	451
		mercury biniodide	491
		pilocarpine	534
		veratrine	651
	bilious	bryonin	179
	rheumatic	colchicine	312
	stitch after	bryonin	179
Pleurodynia		asclepidin	112
		atropine	137
		bryonin	179
		zinc phosphide	671
Pleuropneumonia		asclepidin	112
		bryonin	179
Pneumogastric irritation		cicutine	275
		collinsonin	313
Pneumonia:	treatment		28
		aconitine	38, 42
		antimony arsenate	64
		apocynin	68
		asclepidin	112
		atropine	137
		baptisin	141
		bryonin	179
		cactin	184
		calcium sulphide	218
		capsicin	255
		caulophyllin	257
		cocaine	293
		digitalin	365
		emetine	380
		glonoin	407
		lobelin	479
		pilocarpine	531
		quinine	559
		resorcin	575
		salicylic acid	582
		sanguinarine	588
		sodium benzoate	151
		veratrine	650
	asthenic	benzoic acid	148
		strychnine	637
	catarrhal	arsenic	96
	delirium	hyoscine	429
	double	aspidospermine	115
	of aged	benzoic acid	148
		sanguinarine	588
	suppurative	creosote	335
	typhoid	bryonin	179
		nuclein	511
		sanguinarine	588
		zinc phosphide	671
Podophyllin			547
Podophyllotoxin			547
Poisoning:	acute	mercury	491
	acute: opiate		495
	carbonic acid	apomorphine	71
	malarial	emetine	375
	morphine	atropine	132
	narcotic	apomorphine	71
		atropine	132

Disease	*Phase*	*Remedy*	*Page*
Poisoning:	narcotic	caffeine	193
	ptomaine	pilocarpine	531
	rhus	emetine	375
	septic	baptisia	139
	strychnine	apomorphine	71
		butyl-chloral-hydrate	182
		cicutine	275
Populin			550
Potassium:	arsenate		550
	bichromate		550
	permanganate		551
Pregnancy:	debility	bebeerine	146
		cetrarin	262
		lecithin	468
		nuclein	516
	apprehension	anemonin	59
	nausea	emetine	375
	nervousness	macrotin	485
	pains during	caulophyllin	257
	vomiting	aconitine	28
		aletrin	54
		cerium oxalate	260
		copper arsenite	329
		viburnin	661
Priapism		caffeine	202
		calcium sulphide	218
		camphor monobromide	232
		cannabis indica	237
		hyoscyamine	449
		salicin	582
		veratrine	651
Proctitis		æsculin	49
		chromium sulphate	274
Prolapsus ani		berberine	152
		capsicin	251
		hamamelin	411
	uteri	aletrin	54
		berberine	152
		collinsonin	313
		helonin	416
Prosopalgia		camphor monobromide	232
	syphilis	phytolaccin	526
Prostatitis		aconitine	28
		chromium sulphate	273
		cubebin	337
		eupurpurin	396
	chronic	chimaphilin	269
Prostatorrhea		anemonin	59
		atropine	132, 137
		cantharidin	248
		hyoscyamine	448
		iridin	455
		senecin	602
Prostration (see neurasthenia and debility)			
Protoveratrine			649
Prurigo		aconitine	28
		alnuin	54
		arsenic sulphide	110
		cantharidin	248
		iridin	456
		juglandin	463
		pilocarpine	531

Disease	*Phase*	*Remedy*	*Page*
Pruritus		aconitine	28
		arsenic sulphide	111
		atropine	132, 137
		berberine	152
		brucine	177
		cannabis indica	239
		cicutine	280
		colchicine	302
		gelseminine	400
		helenin	414
		pilocarpine	531
		veratrine	650
		zinc cyanide	667
	vulvae	collinsonin	313
		rhus tox	579
Pseudoleukemia		arsenic	96
		iron	460
Psoriasis		arsenic	96
		arsenic sulphide	110
		cantharidin	248
		iron arsenate	461
		phytolaccin	526
		pilocarpine	531
		salicylic acid	586
		zinc phosphide	667
Puerperal affections (see eclampsia, fever, etc.)			
Pulmonary edema		digitalin	360
		ergotin	382
Purpura		alnuin	54
		anemonin	59
		arsenic	97
		cocaine	296
		hamamelin	411
		hydrastinine	424
Pus formation		calcium sulphide	229
Pyelitis		arbutin	77
		barosmin	145
		cantharidin	248
		chimaphilin	269
		gold	409
Pyelonephritis		arbutin	77
		chimaphilin	269
Pyemia		arsenic	96
		quinine salicylate	559
Pyorrhea alveolaris		calcium sulphide	229
		zinc sulphocarbolate	674
Pyrosis		calcidin	213
		cerium oxalate	260
		cornin	331
		manganese oxide	487

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Quassin			552
Quebrachamine			115
Quebrachine			115
Quinine			559
	arsenate		559
	chocolates		559
	salicylate		559
	tasteless		559
Quinsy (see tonsillitis)		aconitine	28

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Quinsy (see tonsillitis)		echinacea	370

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Rabies (see hydrophobia)			
Raynaud's disease		atropine	132
		glonoin	406
		veratrine	651
Rectum:	affections	aesculin	49
		phytolaccin	526
	atony	berberine	152
	congestion	collinsonin	313
	excoriations of acidity	arsenic	85
	fullness in pregnancy	collinsonin	313
	hemorrhages	hydrastinine	421
	pain	atropine	120, 137
		collinsonin	313
	relaxation	cantharidin	249
	ulcer	cantharidin	249
Reflex irritability		nickel bromide	509
Resorcin			575
Respiratory weakness		picrotoxin	529
	chronic	helenin	413
	endurance	aspidospermine	119
	maladies	camphor monobromide	232
		juglandin	463
	spasm	cicutine	275
Retina detached		pilocarpine	531
Retinitis:	albuminuric	gold	409
Rhein			576
Rheumatic gout		bryonin	179
		colchicine	302
		rhus tox	579
		salicin	582
	polyarthritis	sodium benzoate	151
Rheumatism		acetanilid	27
		acid benzoic	149
		aconitine	41, 45
		agaricin	50
		anemonin	59
		apocynin	68
		arbutin	77
		asclepidin	112
		aspidospermine	119
		atropine	137
		bryonin	180
		calcalith	211
		cannabis indica	239
		caulophyllin	258
		chimaphilin	269
		collinsonin	313
		hamamelin	411
		iron	460
		juglandin	463
		macrotin	484
		nuclein	515
		phytolaccin	526
		resorcin	575
		rhus tox	579
		salicylic acid	587
		sodium benzoate	151
		sodium sulphocarbolate	674

Disease	*Phase*	*Remedy*	*Page*
Rheumatism		veratrine	651
	chronic	bebeerine	146
	gonorrheal	arsenic sulphide	110
	of fingers	bryonin	180
		calcium sulphide	227
	remains in joints	bryonin	180
	sympathetic fever	echinacea	370
	syphilitic	iridin	455
Rhus tox			577
	poisoning	alnuin	54
		echinacea	370
		emetine	380
		lobelin	478
		pilocarpine	531
Rickets		diastase	348
		lecithin	476
		nuclein	511
		zinc phosphide	671
	diarrhea	cotoin	333
Rigid os uteri		caulophyllin	257
		gelseminine	397
		hyoscyamine	447
		lobelin	479
Ringworm		chelidonin	264
		croton oil	336
		pilocarpine	541
Rosacea		arsenic	85
		arsenic sulphide	110
		stypticin	508
Roseola		atropine	137
		calcium sulphide	226
		emetine	375
Rubijervine			649
Rumicin			581
Rumination		arsenic	85

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Salicin			582
Salicylic acid			582
Salivation		agaricin	50
		atropine	120
		geranin	403
Sallowness		alnuin	54
Sanguinarine			588
Santonin			590
Sapremia		salicylic acid	585
Sarcinae		salicylic acid	585
Sarcoma		arsenic	99
Satyriasis		camphor monobromide	230
		salicin	582
		zinc valerate	676
Scabies		calcium sulphide	226
		helenin	413
		phytolaccin	526
Scalp:	tender	bryonin	179
Scaly skin diseases		arsenic	99
Scarlatina		aconitine	28
		arsenic	99
		atropine	137
		baptisin	142
		benzoic acid	149

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Scarlatina		bryonin	180
		calcium sulphide	226
		capsicin	255
		echinacea	370
		pilocarpine	541
		potassium permanganate	551
		rhus tox	580
		salicylic acid	584
		sodium benzoate	151
	angina	baptisin	139
		echinacea	370
		phytolaccin	526
		piperine	546
		salicylic acid	584
Scars		thiosinamine	638
Sciatica		acetanilid	27
		aconitine	28
		apocynin	68
		atropine	137
		codeine	299
		colchicine	312
		colocynthin	318
		croton oil	336
		delphinine	346
		gelseminine	397
		macrotin	484
		narceine	506
		rhus tox	580
		veratrine	650
Scillitin			591
Scleritis		colchicine	312
Sclerosis		barium chloride	145
		benzoic acid	147
	disseminated	arsenic	85
	multiple	ergotin	382
		hyoscine	429
		veratrine	651
Scoparin			617
Scopolia			593
Scopolamine			593
Scorpion:	sting	aconitine	28
		echinacea	370
Scrofula		alnuin	54
		apocynin	68
		arbutin	77
		arsenic iodide	109
		bryonin	179
		calcidin	213
		calcium sulphide	224
		chimaphilin	269
		corydalin	332
		iodoform	453
		iridin	455
		iron iodide	461
		juglandin	463
		menispermin	491
		phytolaccin	526
		podophyllin	547
		stillingin	625
	cerebral irritation	cypripedin	340
	swellings	gold	408
		mercury biniodide	491

Disease	*Phase*	*Remedy*	*Page*
Scurvy		alnuin	54
		atropine	138
		lecithin	470
		manganese	487
		nuclein	511
Scutellarin			601
Scybala		jalapin	462
Sea sickness		acetanilid	27
		atropine	138
		cocaine	295
		copper arsenite	330
		glonoin	404
		pepsin	520
		rhein	576
Senecin			602
Senile decay:	acute	hyoscine	427
	degeneration	zinc phosphide	671
	premature	gold	408
		lecithin	470
		nuclein	511
	tremor	cocaine	295
Sepsis		arbutin	77
		bryonin	179
		echinacea	372
		elaterin	373
		ergotin	393
		nuclein	516
		salicylic acid	582
Serous inflammations		aconitine	28
		bryonin	179
		codeine	300
		mercury	492
	effusions	salicylic acid	582
Serpiginous ulcers		anemonin	59
Sexual atony		brucine	176
		echinacea	370
		gossypin	410
		senecin	602
		yohimbine	664
		zinc phosphide	671
	debility	asparagin	113
		atropine	120
		cannabis indica	237
		cantharidin	244
		cicutine	275
		helonin	417
		piperine	546
		strychnine	634
	irritation	calcium sulphide	218
		camphor monobromide	230
		cypripedin	340
		nickel bromide	510
		populin	550
		salicin	582
		zinc valerate	676
Shock		atropine	120
		brucine	176
		digitalin	365
		glonoin	406
		strychnine	634
Sinuses:	old	benzoic acid	147
Skin diseases		alnuin	54

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Skin Diseases		antimony arsenate	64
		arbutin	77
		arsenic	96
		arsenic iodide	109
		arsenic sulphide	110
		asclepidin	112
		calcalith	208
		calcium sulphide	227
		chelidonin	262
		chimaphilin	269
		corydalin	332
		echinacea	370
		ergotin	393
		hydrastine	417
		hydrastinine	425
		juglandin	463
		nuclein	516
		pilocarpine	531
		podophyllin	547
		rhus tox	577
		rumicin	581
		salicylic acid	582
		veratrine	651
	painful	atropine	120
	suppurative	arsenic sulphide	110
	with menstrual disorder	calcium sulphide	227
		stypticin	508
Sleep:	loss of	caffeine	193
Smallpox		aconitine	28
		atropine	138
		baptisin	142
		calcium sulphide	226
		cocaine	295
		echinacea	370
		pilocarpine	531
		rhus tox	577
		salicylic acid	582
		thiosinamine	638
Snakebites (see venoms)			
Sneezing		arsenic	85
		atropine	138
		calcidin	213
Snuffles:	infants	calcidin	213
Sodium arsenate			85
benzoate			151
salicylate			582
succinate			603
Solanine hydrochloride			604
Solar plexus atony		capsicin	251
Soldiers' marching fatigue		caffeine	193
Somnambulism		hyoscine	427
Somnolence		aconitine	28
		caffeine	200
		leptandrin	477
	icteric	pilocarpine	531
Sore mouth		hydrastine	417
muscles		macrotin	484
nipples		acid benzoate	147
throat		capsicin	251
Sparteine			617
Spasms		aconitine	28
		apomorphine	71

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Spasms		atropine	138
		butyl-chloral-hydrate	182
		camphor monobromide	232
		cicutine	275
		codeine	300
		gelseminine	397
		lobelin	478
		rhus tox	577
	acute	benzoic acid	147
	hysteric	apomorphine	71
		atropine	138
		camphor monobromide	232
		narceine	504
	infantile	emetine	378
	intestinal	atropine	138
	local	cicutine	275
	muscular	cicutine	275
	neck of bladder	atropine	138
	night	hyoscine	429
	nonstriated fiber	atropine	138
	of anal sphincter	atropine	138
	orifices	atropine	138
	palpebral	cicutine	275
	reflex	zinc cyanide	667
	uterus	atropine	138
	worms	santonin	590
Spermatorrhea		anemonin	59
		atropine	138
		avenine	138
		camphor monobromide	232
		cannabis indica	240
		capsicin	255
		collinsonin	313
		cubebin	337
		ergotin	387
		hyoscine	425
		iridin	456
		salicin	582
		strychnine	636
		zinc valerate	676
Sphacelus		baptisin	139
		capsicin	255
Sphincter constrictions		atropine	120
	spasmodic	æsculin	49
		cicutine	275
		collinsonin	313
Spinal pain		acetanilid	27
Spine exhaustion		emetine	375
	hyperemia	croton oil	335
		gelseminine	400
	irritation	aconitine	28
		cicutine	275
	sclerosis	gold	408
	softening	benzoic acid	147
Spleen:	enlargement	berberine	153
		boldine	173
		ergotin	382
		iridin	455
		mercury biniodide	491
		quinine	559
Spongy gums		cetrarin	262
Sputa:	putrid	calcium sulphide	218

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Sterility		aletrin	54
		atropine	120
		gold	408
		lecithin	470
		nuclein	511
		sanguinarine	588
		senecin	602
		viburnin	661
		zinc phosphide	671
Stiffness:	bicyclists'	bryonin	179
Stillingin			625
Stings and bites		apiol	65
Stomach:	dilatation	berberine	153
		papayotin	518
		strychnine	633
	irritable	caffeine	204
		camphor monobromide	232
		cerium oxylate	260
		zinc cyanide	667
Stomatitis		copper arsenite	330
		echinacea	370
		hydrastine	418
		iridin	455
		phytolaccin	526
		rumicin	581
	aphthous	caulophyllin	258
	mothers'	alnuin	54
	ulcerative	echinacea	370
Stools:	dark, offensive	podophyllin	547
	white, offensive	calomel	492
Stramonium			120
Strangury		apiol	65
		arbutin	77
		cannabis indica	240
		cantharidin	244
		chimaphilin	269
		cocaine	295
		codeine	300
		eupurpurin	396
		gelseminine	400
		hyoscyamine	446
Stricture		gelseminine	400
Struma		apocynin	68
		nuclein	516
Strophanthin			626
Strychnine			628
	arsenate		636
	habit		636
	hypophosphite		636
	nitrate		636
	poisoning		636
		curarine	340
		delphinine	346
		lobelin	479
	valerate		636
Styes		anemonin	59
Styptic		benzoic acid	147
Stypticin			507
Subinvolution		berberine	152
		cannabis indica	240
		caulophyllin	258
		ergotin	386

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Subinvolution		stypticin	507
Subsultus		scutellarin	601
Suicide:	impulse to	apomorphine	71
Sunburn		hamamelin	411
Sunstroke		aconitine	28
		atropine	138
		caffeine	200
		glonoin	404
		veratrine	651
Suppuration		baptisin	142
		calcium sulphide	227
		nuclein	511
		quinine	559
Supraorbital pain		bryonin	179
		rhus tox	577
		salicylic acid	582
Sweating:	colliquative	asclepidin	112
		cotoin	333
	unilateral	pilocarpine	531
Sycosis		phytolaccin	526
Syncope		atropine	138
		brucine	177
		camphor monobromide	232
		emetine	375
		glonoin	405
Synechiae		atropine	120
Synovitis		bryonin	179
		rhus tox	577
Syphilis		apocynin	68
		arsenic	103
		arsenic iodide	109, 110
		berberine	152
		corydalin	332
		gold	409
		iodoform	453
		iridin	455
		iron	459
		mercury	492
		nuclein	516
		pilocarpine	537
		podophyllin	547
		stillingin	625
		veratrine	651
	anemia	iron iodide	462
	bone pains	hyoscyamine	447
	hereditary	calcidin	213
	mucous	cantharidin	248
	secondary	chimaphilin	269
		iridin	455
	syphilides	phytolaccin	526

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Tachycardia		cactin	192
Tapeworm		arecoline	84
		iodoform	453
		koussein	468
		papayotin	518
		pelletierine	518
Teething		cypripedin	340
		juglandin	463
		phytolaccin	547

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Teething		rhein	576
		scutellarin	601
	convulsions	gelseminine	397
Temperature:	subnormal	atropine	120
		caffeine	205
		gold	408
		mercury	491
Tenesmus		camphor monobromide	235
		capsicin	254
		gelseminine	393
	rectal	æsculin	49
		collinsonin	313
	vesical	arbutin	77
		hyoscyamine	447
		populin	550
Tetaniform rigidity		cicutine	275
Tetanus		acetanilid	27
		atropine	138
		barium chloride	142
		cannabis indica	240
		cicutine	279
		curarine	340
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